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OBSTETRIC RESPONSIBILITY FOR THE PREVENTION OF FETAL DEATHS*

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WITHIN less than a decade, "maternal welfare" has become an increasingly important phase of public health. Through a better organized nationwide program of education, prospective parents are becoming aware of the advantages of modern obstetric methods. The medical profession and hospital authorities are making determined efforts to provide proper facilities to meet the growing demand for obstetric care in hospitals.

Pediatricians, responsible now for the care of newborn infants in many hospitals, have established simplified routines of infant feeding which satisfy the demands of most babies. Feeding problems in mature infants have been reduced to a minimum. As a result, pediatricians are concentrating their attention upon other problems such as development of a satisfactory routine for the care and feeding of premature infants, prevention and treatment of infections in the newborn, and measures necessary to improve the health and development of babies at birth.

Internists have become much interested in the progress of pregnancy and its effect on the health of women who are the victims of chronic organic diseases and especially those of the cardiovascular system and the kidneys.

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Neuropsychiatrists have long been responsible for the care of individuals handicapped by birth injuries. Failure of efforts to relieve entirely these conditions has directed attention to their prevention. As a result, we now find some neuropsychiatrists intensely interested in obstetric methods and attempting to influence obstetricians in the choice and dosage of drugs and anesthetics used for relief of pain during labor and delivery.

In addition to all this, public health agencies have recently taken a more active interest in maternal welfare. Obstetricians are attempting to comply with the demands of many new public health rules and regulations designed to protect the lives and health of women and their newborn infants.

In other words, obstetricians now find themselves in the position of attempting to satisfy the increasing demands of an enlightened public, specialists in related fields of medical practice and their own local Departments of Health. It is probably fair to state that in no other type of specialty practice has there been manifest, on the part of individuals or health agencies, as much interest in the suitability of methods employed or the results obtained. This may be regarded as a logical development because in the practice of obstetrics a large group of essentially healthy individuals must be subjected to conditions which often involve serious risk to their lives and health.

Obstetricians can hardly fail to be conscious of this increasing demand for perfection in the results of their work. Its effect is a wholesome one in that it is an important factor in forcing us to improve hospital obstetric facilities, to develop new and better methods and to reconsider the logic of certain accepted obstetric procedures.

Interest in this subject led to a recent study of all fetal deaths occurring on the obstetric service at the Woman's Hospital during a five-year period from 1935 to 1939 inclusive. A detailed analysis was made of the causes of these deaths in relation to the health of the mothers during pregnancy, the character and management of their labors and deliveries, and the progress of infants that were born alive but died within one month after birth. The study included all deaths of viable infants born on both our ward and private obstetric services.

This study was undertaken with the purpose of placing emphasis on the more common causes of fetal deaths. It was hoped that by arousing interest in factors which had contributed to failures, management of certain obstetric complications might be improved.

In accordance with the standard of viability which we have used for a number of years, babies were considered nonviable and were excluded from this study, if they weighed less than 1,500 Gm. at birth or were less than 35 cm. in length.

Within the five-year period, 7,661 viable babies were born. Of these, 271 were either born dead or died within one month after birth. The incidence of fetal deaths was therefore 3.5 per cent, or 35 per 1,000 viable births.

In the following 15 tables (Tables I to XV), data resulting from the study of this small series of fetal deaths is summarized.

TABLE I. SUMMARY OF DATA REGARDING 271 FETAL DEATHS OCCURRING AT THE WOMAN'S HOSPITAL DURING THE YEARS 1935 TO 1939 INCLUSIVE

The study included all fetal deaths of viable babies, babies at least 35 cm. in length and weighing not less than 1,500 Gm. (3 pounds 5 ounces) at birth.

Total No. of viable births	7,661
Total No. of fetal deaths	271
Percentage of fetal deaths	3.5

Fetal death rate, 35 per 1,000 viable births.
The 271 babies were born to 269 women (2 sets twins).

HOSPITAL STATUS OF MOTHERS		BABIES WERE DELIVERED BY	
Private	116	Attending surgeons	115
Ward	155	Resident surgeons	122
		Courtesy surgeons	34
Total	271		271

TABLE II. SUMMARY OF PREVIOUS PREGNANCIES AS RECORDED IN THE HISTORIES OF 269 MOTHERS

138 Women had had no previous pregnancies.
131 Women had had 318 pregnancies which were terminated as follows:

Spontaneous abortions	42
Induced abortions	25
Premature deliveries	9
Delivery at term	242
Total	318

Outcome of the 242 babies born at term was as follows: Living babies 207; stillbirths 23; Neonatal deaths 12. The 131 mothers had lost 35, or 16.9 per cent, of babies born at term in previous pregnancies.

Since the 131 women had lost 16.9 per cent of babies born at term in previous pregnancies, it would seem reasonable to expect that an incidence of obstetric complications above average might be encountered during the pregnancies being reviewed in this study.

In the classification of newborn infants, birth weight has come to be recognized as the most reliable single index of prematurity. By this standard, babies weighing less than 2,500 Gm. (5 pounds 8 ounces) at birth are considered to be premature. In Table III, it will be noted that in the series of 271 fetal deaths to be reported, 37 per cent of the babies had birth weights ranging between 1,500 (3 pounds 5 ounces) and 2,500 Gm. (5 pounds 8 ounces) and were therefore classified as premature.

As shown in Table III, approximately one-fifth of the fetal deaths occurred in utero before the onset of labor. About one-half of the babies died either before the onset or during the course of labor. The remaining one-half were born alive but died within the first month of life.

In the past, prematurity has been considered the cause for many neonatal deaths which we now know were due to intrauterine asphyxia and birth trauma. The susceptibility of premature infants to the development of these conditions during labor and delivery is now well recognized. Because a very high percentage of neonatal deaths in premature infants are due to birth trauma and asphyxia, the responsibility of an obstetrician does not end with the delivery of a living premature infant.

In New York a large committee of pediatricians and obstetricians appointed by the Commissioner of Health is studying methods for prevention of newborn premature infant mortality. Presuming that the problem was a pediatric one, the committee was placed under the chairmanship of an enthusiastic pediatrician. After many months of collecting and analyzing statistics, the unavoidable conclusion has been reached that the problem is essentially an obstetric one.

TABLE III. DISTRIBUTION OF 271 FETAL DEATHS AS TO WEIGHT AT BIRTH AND TIME OF DEATH IN RELATION TO LABOR

TIME OF FETAL DEATH	WEIGHT AT BIRTH		TOTAL	PER CENT
	1,500 TO 2,500 GM.	2,500 GM. AND OVER		
Ante partum	25	31	56	21
Intra partum	15	61	76	28
Neonatal	60	79	139	51
Total	100	171	271	100
Per cent	37	63	100	--

It is a well-known fact that when babies are too large at time of delivery, the risk of birth injury to both mothers and their babies is increased. Table IV is a summary of the birth weights of 70 of the 271 babies in the series that were of a size recognized as above average normal when delivered.

TABLE IV. SUMMARY OF BIRTH WEIGHTS OF OVERSIZED BABIES IN SERIES OF 271 FETAL DEATHS

BIRTH WEIGHT	TIME OF DEATH			TOTAL
	ANTE PARTUM	INTRA PARTUM	POST PARTUM	
3,500 to 4,000 Gm. (7 pounds 11 ounces to 8 pounds 13 ounces)	6	20	21	47
4,000 to 4,500 Gm. (8 pounds 13 ounces to 9 pounds 15 ounces)	4	6	6	16
4,500 to 5,000 Gm. (9 pounds 15 ounces to 11 pounds 0 ounces)	2	3	1	6
5,000 Gm. (11 pounds 0 ounces).			1	1
Total	12	29	29	70

During the first month of life, prematurity and conditions associated with it, constitute by far the most important predisposing factor in the causation of infant deaths. From reliable statistics it has been estimated that the chance for survival of a baby born alive at term is more than 15 times better than that for a premature infant.

Table V is a summary of the incidence of fetal deaths in the various weight groups which occurred at the Woman's Hospital during the years 1938 to 1940, inclusive. For safety to the baby, it demonstrates the importance of prolonging intrauterine life of the fetus to as near full term as possible.

TABLE V. SUMMARY OF OUTCOME OF PREMATURE BABIES BORN AT THE WOMAN'S HOSPITAL FROM 1938 TO 1940, INCLUSIVE, IN RELATION TO BIRTH WEIGHTS

WEIGHT AT BIRTH GM.	NUMBER	DEATHS	PER CENT
1,500 to 1,750	50	14	28.0
1,750 to 2,000	58	11	18.97
2,000 to 2,250	97	12	12.37
2,250 to 2,500	166	7	4.22
Total premature births (1,500-2,500 Gm.)	371	44	11.86
Total term births (2,500 Gm. and over)	4,802	56	1.17

With improvements in the routine care of premature babies, some neonatal deaths can probably be prevented. However, the most effective means of reducing the incidence of these deaths is to reduce the incidence of premature births. This is not easy to accomplish as no cause can be found for a considerable percentage of prematurely terminated pregnancies.

In the prevention of premature fetal deaths, contraception and sterilization have a definite place. In some women with conditions such as chronic cardiovascular disease, chronic nephritis, and diabetes, which predispose to premature birth, pregnancy should be prevented. For any woman who has tuberculosis, syphilis, or subnormal physical health from any cause, pregnancy should be postponed to improve the chances for a normal pregnancy and a healthy child.

As our knowledge of the essential requirements for the health of a woman in the prenatal period increases, means may be found to reduce the incidence of premature births. Certainly women should be encouraged to follow a good routine of rest and hygiene during pregnancy with the hope of preventing premature delivery as well as other complications.

Table VI is a summary of causes of the 271 fetal deaths. Diagnosis of the cause of death was established by autopsy in 203, or 75 per cent, of the babies in the series.

TABLE VI. SUMMARY OF CAUSES OF THE 271 FETAL DEATHS

CAUSE OF DEATH	ANTE PARTUM	INTRA PARTUM	NEONATAL	TOTAL	PER CENT
Trauma		30	49	79	29
Intrauterine asphyxia	16	17	11	44	16
Asphyxia and trauma	30	19	32	81	30
Congenital malformations	7	6	23	36	13
Miscellaneous	3	4	24	31	12
Total	56	76	139	271	100
Per cent	21	28	51	100	---

75 per cent of deaths were due to trauma or asphyxia or both.

From Table VI it will be noted that trauma and asphyxia were by far the most important factors in the causation of the 271 deaths. Briefly it may be stated that trauma and asphyxia were responsible for 75 per cent of the deaths, congenital malformations for 13 per cent and miscellaneous conditions for the remaining 12 per cent.

Tables VII, VIII, and IX contain a detailed account of the causes for the 271 fetal deaths.

TABLE VII. SUMMARY OF CAUSES OF THE 271 FETAL DEATHS

CAUSE OF DEATH	ANTE PARTUM	INTRA PARTUM	NEONATAL	TOTAL
Trauma:				
Intracranial hemorrhage		2	19	21
Tentorial tear		8	1	9
Intracranial hemorrhage and tentorial tear		18	25	43
Hemorrhage, abdomen and intestines		1		1
Hemorrhage, abdomen and lungs			1	1
Hemorrhage adrenals			2	2
Ruptured liver			1	1
Cervical dislocation		1		1
Total		30	49	79
Intrauterine Asphyxia:				
Abruptio placentae	7	3	2	12
Placenta previa	1	1	6	8
Cord around neck	6	11	1	18
Prolapsed cord		2	2	4
Abnormal placenta	2			2
Total	16	17	11	44
Intrauterine Asphyxia and Trauma:				
Congestion and edema, brain	1	1	16	18
Congestion and edema, brain and other organs		2	6	8
Cause of asphyxia?	29	16	10	55
Total	30	19	32	81
Congenital Malformations*	7	6	23	36
Miscellaneous*	3	4	24	31
Total	56	76	139	271

*Tables VIII and IX give a detailed list of congenital malformations and miscellaneous conditions resulting in fetal deaths.

In Table VII it will be noted that 55 fetal deaths were classified as due to intrauterine asphyxia and trauma although the exact causes of these deaths were never determined. Of these 55 deaths, 29 occurred before the onset of labor and 27 of the 29 babies were macerated when delivered. Although autopsies were done on 21 of the 29 babies the exact causes of death could not be determined. One mother had eclampsia, one epilepsy, and one cardiac disease. In 26 of the 29 mothers no maternal cause could be discovered which might predispose to fetal death. Sixteen of the 29 babies were definitely premature.

Sixteen intrapartum and 10 neonatal deaths of undetermined cause were also included with deaths due to trauma and intrauterine asphyxia. Autopsies were done following only 7 of these 26 deaths. Before delivery was attempted 14 of the 26 babies were either in distress or dead. A study of the circumstances which attended the labors and deliveries of these 26 babies seemed to justify definitely their inclusion among the babies that died from birth trauma and asphyxia.

In Table IX it will be noted that 11 of the 31 deaths were the result of infection and that of the 11 deaths from infections 9 were from infections of the lungs. Some of these deaths were probably due to asphyxia and intrauterine aspiration of infected amniotic fluid.

TABLE VIII. SUMMARY OF CONGENITAL MALFORMATIONS RESULTING IN 36 OF THE 271 FETAL DEATHS

DIAGNOSIS	NO.	DIAGNOSIS	NO.
Malformation of heart	4	Abnormal trachea and bronchi	3
Mongolism	2	Diaphragmatic hernia	3
Hydrocephalus	6	Atresia duodenum	1
Hydrocephalus, hypertrophic bladder and bilateral hydroureters	1	Atresia colon	1
Hydrocephalus, imperforate anus, absence of both kidneys	1	Pyloric stenosis. Malformation of chin and hand	1
Anencephalus	3	Ectopia of viscera	1
Spina bifida	1	Malformation both kidneys	1
Anencephalus and spina bifida	2	Hypoplasia adrenals	1
Anencephalus, absence of both adrenals and right kidney	1	Cleft palate, anisophthalmy	1
		Harelip, aspiration	1
		Massive umbilical hernia (eventration of viscera)	1
Total	21	Total	15

TABLE IX. SUMMARY OF MISCELLANEOUS CONDITIONS RESULTING IN 31 OF THE 271 FETAL DEATHS

CAUSES OF DEATHS	TIME OF FETAL DEATHS			
	ANTE-PARTUM	INTRA-PARTUM	NEONATAL	TOTAL
Prematurity			4	4
Postmaturity	1			1
Erythroblastosis	2		4	6
Bronchopneumonia			4	4
Bronchopneumonia and atelectasis			3	3
Bronchopneumonia and aspiration			1	1
Lobar pneumonia agranulocytosis			1	1
Icterus gravis			2	2
Anemia, icterus, splenomegaly			1	1
Edema neonatorum, parenchymatous, degeneration of internal organs			1	1
Gastroenteritis			1	1
Status thymolymphaticus		1	1	2
General peritonitis			1	1
Aspiration amniotic fluid		3		3
Total	3	4	24	31

From study of Tables VII, VIII, IX, and X, it is apparent that the best opportunity to reduce the incidence of fetal deaths is in the prevention of birth trauma and fetal asphyxia, the result of labor and delivery.

In this series of 271 fetal deaths, 215 (intrapartum 76, neonatal 139) occurred during the course of labor or within one month after birth. Of these 215 deaths, 158, or 73.4 per cent, nearly three-fourths, were due to trauma and asphyxia.

Much has been written as regards the dangers of birth injury to babies from operative interference. In the light of our present knowledge too little emphasis has been placed upon damage resulting to babies and mothers from unduly prolonged pressure of labor and the opportunity which not infrequently comes to save babies by timely and skillful operative interference.

In a study[1] of the comparative results of spontaneous delivery and delivery by so-called prophylactic forceps at the Woman's Hospital,

TABLE X. CONDITION OF BABIES AT TIME OF DELIVERY IN RELATION TO BIRTH WEIGHT AND CAUSES OF FETAL MORTALITY IN THE 76 INTRAPARTUM AND 139 NEONATAL DEATHS

BIRTH WEIGHT AND CONDITION AT TIME OF DELIVERY	CAUSE OF FETAL DEATH					TOTAL	PER CENT
	TRAUMA	INTRA-UTERINE ASPHYXIA	ASPHYXIA AND TRAUMA	CONGENITAL MALFORMATIONS	MISCEL.		
1,500 to 2,500 Gm.							
Normal	13	8	13	9	9	52	69
In distress	6	2	5	0	2	15	20
Dead	1	3	2	2	0	8	11
Total	20	13	20	11	11	75	100
2,500 Gm. and over							
Normal	38	4	16	15	13	86	61
In distress	15	3	9	1	3	31	22
Dead	6	8	6	2	1	23	17
Total	59	15	31	18	17	140	100
All babies—1,500 Gm. and over							
Normal	51	12	29	24	22	138	64
In distress	21	5	14	1	5	46	21
Dead	7	11	8	4	1	31	15
Total	79	28	51	29	28	215	100

we were interested to find that in a large series of normal cases, fetal mortality was 50 per cent less after the prophylactic forceps method of delivery.

A discussion of the causes and prevention of fetal deaths would hardly be complete without consideration of modern methods of analgesia and anesthesia. Common faults in the use of these measures could be found in the records of some of the patients delivered in this series. To what extent pain-relieving drugs and anesthetics had contributed to the causes of death was not easy to determine. However, it was obvious that in some instances analgesic drugs may have been given too early in labor and that oxytoxic drugs had then been employed to counteract their depressing effect on uterine contractions. In other cases rather excessive amounts of analgesic drugs had been used in divided doses at too short intervals to determine whether the preceding doses might be effective. After some inefficient labors, perhaps in part the result of too much analgesia, difficult deliveries had to be conducted too early in labor with the hope of saving babies already in distress.

It is our conviction that, for safety, administration of analgesic drugs should be postponed until labor is well established and that the dosage should be moderate, especially in premature labors. If methods for using local instead of general anesthesia can be perfected and used more extensively, danger from this source can be reduced.

It was rather astonishing to find as shown in Table X, that in the 158 intrapartum and neonatal deaths in this series from trauma and asphyxia, 66, or 41.7 per cent, of the babies were either in distress or dead before delivery was attempted. From this it may be assumed that more than four out of ten of these fetal deaths were the result

of labor rather than the delivery. Approximately 85 per cent of the 158 babies were eventually delivered by operative means.

A study of the records shows that many of these deaths occurred in unduly prolonged labors, and labors that failed to progress because of faulty positions of the presenting part, abnormal presentations and cephalopelvic disproportion that was discovered too late in labor. Timely operative interference would almost certainly have saved the lives of some of these infants.

Tables XI and XII show the methods of delivery employed in the 56 cases with antepartum death of the fetus and the 215 cases in which the fetus died during labor and delivery or in the neonatal period.

TABLE XI. METHOD OF DELIVERY EMPLOYED IN RELATION TO CAUSES OF THE 56 ANTE-PARTUM FETAL DEATHS

METHOD OF DELIVERY	CAUSE OF DEATH				TOTAL
	INTRA-UTERINE ASPHYXIA	ASPHYXIA AND TRAUMA	CONGENITAL MALFORMATIONS	MISCEL.	
Spontaneous	7	22	6	2	37
Forceps					
Low	1				1
Prophylactic low	2	3			5
Mid	1		1	1	3
Breech					
Extraction		1			1
Version and extraction	2	1			3
Cesarean section					
Classical	1				1
Cervical	2	2			4
Vaginal hysterotomy		1			1
Total	16	30	7	3	56

TABLE XII. METHOD OF DELIVERY IN RELATION TO CAUSES OF 215 FETAL DEATHS IN 76 INTRAPARTUM AND 139 NEONATAL DEATHS

METHOD OF DELIVERY	CAUSE OF FETAL DEATHS					TOTAL	TOTAL
	TRAUMA	INTRA-UTERINE ASPHYXIA	ASPHYXIA AND TRAUMA	CONGENITAL MALFORMATIONS	MISCEL.		
Spontaneous	10	1	13	6	8	38	38
Forceps							113
Low	11	6	7	4	6	34	
Prophylactic low	15	5	3	6	6	35	
Mid	18	5	9	5	4	41	
High	2		1			3	
Breech							35
Delivery		1	1			2	
Extraction	12	1	3	2		18	
Version and extraction	9	2	2	1	1	15	
Cesarean section							29
Classical		1	1			2	
Cervical	1	6	7	4	1	19	
Extraperitoneal	1		2		2	5	
Porro			2	1		3	
Total	79	28	51	29	28	215	215

TABLE XIII. PRESENTATION AND METHOD OF DELIVERY EMPLOYED IN THE 158 INTRAPARTUM AND NEONATAL DEATHS RESULTING FROM TRAUMA AND ASPHYXIA

PRESENTATION	SPON.	METHOD OF DELIVERY											TOTAL
		FORCEPS				BREECH			CESAREAN SECTION				
		LOW	PRO. LOW	MID	HIGH	DEL.	EXT.	VERS. EXT.	CLASS.	CERV.	EXTRAP.	PORRO	
Vertex													
O.A.	17	12	22	10	1			1			1		64
O.P.	3	7	1	10	2			3		2	1		29
O.T.	2	5		11						1			19
Brow				1				1					2
Face								1					1
No record	2							2		3			7
Breech						2	16			3	1		22
Transverse								5				1	6
No record									2	5		1	8
Total	24	24	23	32	3	2	16	13	2	14	3	2	158
Perineal incision	7	13	22	26	1		10	2					81

Rotation of head in occiput posterior and transverse arrest: spontaneous 18, manual 3, Kielland 12, Scanzoni 8, total 41. 1 delivered as occiput posterior.

Table XIII is a record of presentation and method of delivery employed in the 158 cases in which death of the fetus occurred during labor and delivery or in the neonatal period as a result of trauma and asphyxia.

Table XIV is a record of the indications and types of operations employed in the 35 cases delivered by cesarean section.

TABLE XIV. INDICATIONS AND TYPE OF OPERATION EMPLOYED IN THE 35 BABIES DELIVERED BY CESAREAN SECTION

INDICATIONS	TYPE OF OPERATION					TOTAL
	CLASS.	CERV.	EXTRA-PERIT.	PORRO	VAGINAL	
Placenta previa	1	8		1		10
Abruptio placentae	1	1				2
Cephalopelvic disproportion		4	2			6
Abnormal presentation						
Breech		1	1			2
Transverse		1		1		2
Cervical dystocia		1	2			3
Fetal distress		2				2
Cardiac disease		1				1
Myomas				1		1
Failure of induction					1	1
Previous cesarean	1	4				5
Total	3	23	5	3	1	35

Time of fetal deaths: Antepartum 6, intrapartum 8, neonatal 21, total 35.
Condition of babies before operation: Normal 22, in distress 7, dead 6, total 35.
Weight of babies: 1,500 to 2,500 Gm. 8, 2,500 Gm. and over 27, total 35.

Table XV shows the age at time of death of 139 babies that died within one month after birth. Forty-three per cent of these babies weighed less than 2,500 Gm. at birth and were therefore classified as premature. Nearly three-fourths of the neonatal deaths occurred within forty-eight hours after birth.

TABLE XV. DISTRIBUTION OF THE 139 NEONATAL DEATHS IN RELATION TO BIRTH WEIGHT AND AGE AT TIME OF DEATH

WEIGHT OF BABIES AT BIRTH	TIME OF NEONATAL DEATHS			TOTAL	PER CENT
	UNDER 24 HOURS	FROM 24 TO 48 HOURS	FROM 48 HOURS TO 1 MONTH		
1,500 to 2,500 Gm.	35	11	14*	60	43
2,500 Gm. and above	41	11	27	79	57
Total	76	22	41	139	100
Per cent	55	16	29	100	--

*Includes one hydrocephalic baby that lived 105 days.

DISCUSSION

In the analysis of this small series of fetal deaths, it has been obvious that many of our failures resulted from lack of success in handling some rather common obstetric conditions and complications.

In the past few years, some of our methods of handling certain obstetric complications have been gradually revised with the hope of increasing safety to mothers and avoiding some of the unfortunate

results represented by types of cases contained in the series that has been analyzed for this report. In studying the 269 labors and deliveries which resulted in the 271 fetal deaths, it was difficult to avoid the impression that our failures were rarely due to what seemed improper choice of obstetric procedures to fit the cases, but that they were frequently the result of having applied these procedures too late in the course of labor.

An obstetric complication presenting a problem which not infrequently tests the judgment and skill of every obstetrician, is the patient in whom the cervix only partially dilates or fails to dilate as labor progresses. If the cervix dilates slowly, fetal distress may manifest itself before vaginal delivery is safe or possible. Before the onset of labor it is not easy to predict, with any degree of certainty, that this complication may arise. Various factors such as cephalopelvic disproportion, abnormal presentations and faulty positions of the presenting part are believed to predispose to its occurrence. However, in some women no cause can be found for this complication.

It is usually supposed that for some reason uterine contractions are either inefficient or that the cervix has some inherent anatomic or physiologic qualities which do not allow dilatation to occur. In some of these patients the quality of labor is good and obstetricians find reason to interfere when they decide that, after a satisfactory test of labor, delivery of a living baby by vagina is improbable. Other patients present a much more perplexing problem in that they have a true primary uterine inertia and some of their babies will show signs of fetal distress before uterine contractions have been sufficient in frequency or strength to constitute a legitimate test of labor.

Murphy's[2] observations with the tocograph may explain the reason for development of fetal distress in this type of labor. He has found that in the presence of primary uterine inertia, the uterine musculature sometimes fails to relax completely between contractions. A continued uterine muscular tonicity is the result, and it is possible that the baby suffers from a prolonged low grade anoxemia from interference with placental circulation. Eventually, before vaginal delivery is possible, death of the fetus in utero may occur.

It is interesting that this same complication, failure of the cervix to dilate, may or may not recur in subsequent labors in the same patient.

In our experience, methods recommended to correct difficulties encountered in these cases are not very successful. Obstetricians interested in the mechanism of labor in relation to pelvic architecture are convinced that means will be found to correct factors predisposing to uterine inertia and failure of the cervix to dilate. Endocrinologists are hopeful that they may soon have hormone products which will safely relieve uterine inertia. However, until an effective means is discovered to increase the safety of delivery of these patients by vagina and to prevent fetal deaths, the question is raised as to whether cesarean section can be made a sufficiently safe procedure to justify its use in such circumstances.

At the Woman's Hospital we are convinced that either cervical or extraperitoneal cesarean section skillfully performed in a proper ob-

stetric environment is the safest method of delivery for both mothers and babies in some of these cases. Considerable obstetric judgment is required to decide whether and when these patients should be delivered by cesarean section. Faulty judgment may result in unnecessary cesarean sections or injured babies because delivery by the suprapubic route has been too long delayed.

In some patients with incompletely dilated cervices, if delivery becomes necessary in the interests of either the mother or baby, single or multiple cervical incisions are sometimes useful. However, this procedure cannot be employed without some danger of excessive bleeding and the risk of injury to important adjacent anatomic structures. This method should certainly not be used unless the head is well in the pelvis and the cervix is well thinned out and considerably dilated.

In 58 (26.9 per cent) of the labors in this series, which resulted in intrapartum or neonatal deaths, the fetal head engaged in an occipitoposterior position and had failed to rotate completely when delivery was attempted. In 33, the head was still in an occipitoposterior position, and in 25 it had rotated to a transverse position when delivery was undertaken. Eighteen or more than one-third of the 58 babies were in distress or dead before the decision to interfere had been reached. Twenty-seven of the 58 labors were prolonged as regards the first, the second, or both stages of labor.

In all that has been written regarding so-called conservative obstetrics, no condition has received more attention than occipitoposterior position. The advice has invariably been to leave the occiput posterior to nature, with the assurance that she would rarely require assistance if given sufficient time.

In former days when many women were delivered in their homes or in hospitals with inadequate obstetric facilities, this was undoubtedly sound obstetric teaching. However, in these days, when a high percentage of women are being delivered in well-equipped hospitals by expert obstetricians or under their supervision, will the practice of leaving all occiput posteriors to nature still yield the best results that can be had? If such labors progress well and the babies show no signs of distress, the treatment should be no different than that for anterior positions. However, if all women with occipitoposterior positions are carefully followed during the course of their labors, we are convinced that it is possible to select a certain small percentage in which timely operative interference is likely to be less harmful to the mothers and their babies than continuation of labors which are progressing too slowly.

If we are to prevent fetal deaths from conditions associated with occipitoposterior positions, the indication for operative interference should be unsatisfactory progress of labor rather than fetal distress. The records show that if this rule had been followed some of the fetal deaths in this series might have been avoided.

Twenty of the fetal deaths in this series occurred in women treated for placenta previa and premature separation of normally situated placentas. For patients with placenta previa who come under observation before the cervix has dilated and in those in whom considerable

placenta is implanted in the lower uterine segment, most obstetricians are now agreed that cesarean section is the safest method of delivery. In our experience, delivery by the abdominal route combined with adequate replacement of blood loss and strict precautions against infection have markedly reduced the incidence of mortality from this complication in both mothers and babies.

In the treatment of abruptio placentae, we are called upon to treat a mild form in which simple rupture of the membranes and occasionally a hydrostatic bag yield satisfactory results, and the severe form which must be regarded as one of the most serious complications of pregnancy. In the hands of the most expert obstetricians, the severe form is attended by maternal mortality of at least 6 per cent and a high incidence of fetal deaths. Difference of opinion still exists as to the best method of treatment for this severe form. Some obstetricians favor the use of the Beck binder or the Spanish windlass and delivery by vagina. It is agreed that success in treatment of the severe form will depend upon control of bleeding and emptying the uterus as soon as possible. In our experience prompt cervical cesarean section offers the most logical and safest means of accomplishing both of these objectives. Incidentally this method is a lifesaving measure for some babies that would be lost in delivery by the vaginal route.

A considerable percentage of fetal deaths in this series resulted from unsuccessful management of labors and deliveries complicated by faulty positions of the presenting part, abnormal presentations of the fetus and cephalopelvic disproportion, the result of contracted pelvis or oversized babies.

It is not within the scope of this presentation to attempt to discuss the faults in management of all these varied conditions and complications which were responsible for many of the fetal deaths in the series that has been reported. Suffice it to say that results of treatment would have been better in some instances if certain important procedures had been followed.

Perhaps the most valuable obstetric contribution of this generation for safety of mothers and their babies has been the development and perfection of the stereoscopic method of roentgen pelvimetry. It offers a precise means for determining the size and conformation of the bony pelvis. By use of this diagnostic method, it is possible to predict with considerable accuracy what may be expected during the course of labor and as to whether delivery by vagina is possible or safe. By its use the decision to deliver certain patients by cesarean section can be made without the increased risk of operation after a prolonged test of labor.

The safety of a patient during labor and delivery could be promoted if obstetricians would make use of roentgen studies more frequently to check diagnosis when uncertainty exists as to the position and presentation of the fetus and when there is any question as to whether delivery by vagina is possible or likely to be attended with unjustifiable difficulties.

Prevention of tragic results in the outcome of labors and deliveries complicated by unusual positions of the presenting part, abnormal presentations or cephalopelvic disproportions require careful observa-

tion of the progress of labor. The treatment of such patients should be carried on under the strict supervision of obstetricians who have had sufficient training and experience to know when interference is likely to yield better results than a continuation of labor. Results of the study that has been reported offer conclusive evidence that the choice of the optimum time for interference is just as important as the selection of a proper operative procedure to fit the case.

Twenty years ago it was not uncommon for an obstetrician to accept conditions and to adopt a method of delivery which was sure to result in a stillborn baby. This was sometimes based on the fact that "the patient was young and could try again." On occasion this course was followed in face of conditions which were likely to repeat themselves in subsequent pregnancies.

In recent years, we have been much interested in the prevention of maternal birth injuries. Most of these injuries are now preventable or can be successfully relieved by vaginal plastic surgery. However, perhaps the most serious birth injury in its effect on the health and happiness of a woman, is the emotional injury which comes through loss of a baby at birth and particularly her first. If a woman loses her first baby and for any reason is unable to conceive again, the result is often a tragic one. If she loses the first child, success in subsequent pregnancies never seems to provide sufficient compensation for the initial loss.

Conditions associated with pregnancy and particularly the first probably constitute the most profound emotional experience which comes to a woman within her span of life. It is probably fair to state that obstetricians have underestimated the seriousness of an unfortunate outcome of pregnancy from the emotional standpoint.

The medical profession is gradually learning the importance of emotional disturbances in relation to physical health. In the future, obstetricians may acquire a better understanding of the extent to which success in their efforts is likely to protect the health of women who suffer indirectly from emotional birth injuries.

SUMMARY

1. The causes of 271 fetal deaths that occurred on the obstetric service at the Woman's Hospital in a five-year period have been reviewed as to cause in relation to labor, methods of delivery, and certain aspects of maternal health.

2. Analysis of this series of fetal deaths showed that approximately one-fifth occurred in the ante-partum period, a little more than one-fourth during the course of labor, and about one-half within one month after birth.

3. Prematurity was the outstanding predisposing cause for these fetal deaths, and birth trauma and intrauterine fetal asphyxia were by far the most important actual causes of death.

4. Study of the causes of deaths reveals little that could have been done in either the ante-partum or neonatal periods to prevent their occurrence. It is obvious that our results can and must be improved by more judicious handling of women during labor and delivery.

5. Skillful and timely operative interference will reduce the incidence of birth injuries to some babies that survive as well as to those that die.

6. Provided women can be delivered in a good obstetric environment by skillful obstetricians, or under their direction, there is reason to believe that more babies and mothers will be injured by undue prolongation of labors that fail to progress than by timely operative interference.

7. It is possible that too much obstetric analgesia and anesthesia added to other contributory causes for intrauterine fetal asphyxia may be responsible for some fetal deaths or injured babies.

8. With widespread interest in obstetric results, it behooves obstetricians to reconsider their methods and to determine whether the accepted so-called conservative procedures can still always be depended upon to yield the best results.

9. Experience has shown that skillful application of the newer operative obstetric procedures for the protection of either mothers or their babies, have invariably reduced the hazards of labor and delivery for both. Results of the use of prophylactic forceps, and cesarean section for placenta previa, provide convincing evidence of the truth of this statement.

10. At least three-fourths of all fetal deaths, within the first month of life, are due to obstetric causes. Responsibility for their prevention is obstetric, in that it involves essentially prevention of premature births and management of labors and deliveries in ways to prevent fetal trauma and intrauterine asphyxia.

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Virulent *S. pallida* are discharged by the syphilitic woman into the vagina in the presence of local lesions early or chronologically "late" (more than four years' duration) in the course of the disease as a relapsing phenomenon. In the absence of such lesions, they are discharged only through the menstrual blood of the early syphilitic, or from an abnormal appearing cervix, in which instance it is probable that lesions are present within the cervical os or uterus.

Infectiousness through the vagina is periodically recurrent rather than continuously present in the syphilitic woman and depends upon the presence or absence of local lesions. The physiologic secretions are not infectious.

No data can be given as to the absolute end point of cervical relapse, and no estimate of the frequency of this relapse is available. In the author's series, infectious cervical relapse was found to have occurred at least six and one-half years after definite onset of the disease.

C. O. Maland

THE COMMON ETIOLOGY OF ERYTHROBLASTOSIS AND TRANSFUSION ACCIDENTS IN PREGNANCY*

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THE purpose of this communication is to call attention to the common etiology of two pathologic phenomena, the causes of which until recently have been obscure. These two apparently unrelated phenomena are erythroblastosis fetalis and certain transfusion accidents occurring in pregnancy. As will be explained in detail below, the etiology of erythroblastosis fetalis resides in an immunologic incompatibility between the fetus and the mother. In other words, there is present in the fetal red blood cells an antigen inherited from the father which is lacking in the mother. This antigen diffuses from the child into the mother's circulation, stimulating the formation of destructive antibodies. These antibodies like other maternal antibodies (for example diphtheria antitoxin) also diffuse readily into the fetal circulation where they can attack the red blood cells which contain the antigen, thereby causing erythroblastosis.

Should such a mother need a transfusion and should the transfused blood contain the antigen referred to, the destructive antibodies (agglutinins) in the mother's circulation agglutinate and hemolyze the transfused blood, thereby causing oliguria or anuria with its so often fatal consequences. These reactions occur between bloods of the same group and in spite of apparently compatible cross-matching.

This concept was developed from the following series of studies.

Atypical agglutinins have previously been found by Levine and Stetson,[1] among others.[2, 3] In their case of a transfusion accident following the delivery of a macerated fetus, the origin of the atypical agglutinin was for the first time suggested to be the immunization of the mother by the baby. According to their theory, the baby inherits a dominant blood property from the mother which is lacking in the father. The hypothesis that this immunization may also take place in certain cases of pregnancy with complications other than the retention of a dead fetus has also been advanced.[4]

In January, 1940, Landsteiner and Wiener[5] reported on an agglutinin which was developed in rabbits by the injection of blood from the *Macacus rhesus* monkey. When tested with human bloods this agglutinin demonstrated the presence of a new substance in human red blood cells which they called the Rh factor (Rh from rhesus). It has since been found that about 86 per cent of all human bloods[6] contain this factor (these are called Rh positive), and the remaining 14 per cent do not contain it (Rh negative). The agglutinin is called the anti-Rh agglutinin.

This agglutinin was first reported by Levine, Katzin, and Burnham[7] to be the destructive antibody responsible for the several manifestations of erythroblastosis. As stated by them, "one may assume that the (anti-Rh) agglutinins in the mother's circulation under certain conditions are capable of penetrating the placental barrier so that these antibodies, by their continual action on the blood cells and perhaps tissue cells of the fetus, induce erythroblastosis fetalis."

*Read, in part, at a meeting of the Section of Obstetrics and Gynecology, New York Academy of Medicine, May 27, 1941.

All of the serologic studies in these cases were carried out by Dr. Philip Levine.

Stated in another way, when an Rh negative woman carries in her uterus an Rh positive baby, in certain cases the baby's blood can stimulate the mother to form the anti-Rh agglutinin. This antibody, in turn, is able to pass back through the placenta and destroy the baby's Rh positive blood, thereby causing erythroblastosis. Should the mother be transfused with Rh positive blood, the agglutinin can agglutinate and destroy the transfused blood, the hemoglobin of which blocks the kidneys causing oliguria or anuria. This explanation of the pathogenesis of erythroblastosis has received statistical corroboration in a forthcoming paper.[8]

It should be noted, however, that there are exceptions[7] to this rule, since in certain cases of erythroblastosis the mother's blood also is Rh positive. These are not thought to be exceptions to the theory of immunization but rather to the Rh factor since other blood factors may be involved.

The association of erythroblastosis and transfusion accidents was first suggested by the following case* which was observed in June, 1940.

CASE REPORTS

CASE 1.—Mrs. G. B., aged 32 years, had had one normal pregnancy terminated by forceps delivery (baby 9 pounds 9 ounces; no jaundice), and two spontaneous abortions. She was first seen in consultation because labor pains had stopped after fifteen hours of active labor at term; pain severe enough to disturb respiration had appeared in the right upper quadrant; and the fetal heart sounds had disappeared. The baby seemed large, the fetal head was not engaged, and the cervix was 1½ fingers dilated with a long uneffaced canal. With the diagnosis of a possible early rupture of the uterus, a cesarean section was performed. No rupture of the uterus was present and no cause for the pain in the right upper quadrant was found upon palpation of the liver and gall bladder. The baby was dead and weighed 10 pounds 7 ounces. The possibility of erythroblastosis was considered. This clinical impression was gained from the suggestion of edema about the neck and the absence of any more obvious cause for the stillbirth. No blood studies or autopsy were done.

Because of moderate anemia before operation (hemoglobin 60 per cent; red blood count 3,180,000) a 500 c.c. blood transfusion was given during and after the operation by the Baxter citrate method. The husband was used as a donor since both his blood and the patient's blood were of Group A (II Moss), and the cross-matching was satisfactory using the Landsteiner technique. A second transfusion (350 c.c. of Group A blood) was given that same evening because of symptoms suggestive of but not entirely characteristic of surgical shock. The following morning the patient was intensely jaundiced. Diminution of urinary output began on the first day postoperative, the patient excreting 350 c.c. in the first twenty hours after operation, only 3 drops in the next 11 hours, and only 60 c.c. in the following 24 hours. Urinary excretion improved somewhat thereafter but in only one 24-hour period did it exceed 500 c.c. (645 c.c. on the fourth day postoperative).

A third transfusion (400 c.c. of Group A blood) was given on the afternoon of the first postoperative day because of marked anemia (hemoglobin 46 per cent; red blood count 2,300,000). After temporary improvement and in spite of the absence of bleeding the patient became progressively more anemic (hemoglobin 40 per cent; red blood count 2,080,000 on the seventh day postoperative). Hence,

*This case, together with those which follow, largely formed the basis for the theory and have been previously reported in less detail elsewhere.[7]

a fourth transfusion (500 c.c. Group A blood) was given on the seventh day, and for the first time the transfusion was followed by an obvious reaction, namely chill and fever.

The patient became progressively weaker, developed a unilateral parotitis, and died early in the morning of the ninth day postoperative.

The likelihood of erythroblastosis fetalis being the correct diagnosis in this case as well as the association of erythroblastosis with the transfusion accident were strengthened by the similarity between the above case and one which occurred in 1938 (Case 2), with which my contact was mostly indirect.

CASE 2.—Mrs. J. B., aged 30 years, physician's wife, had had one previous pregnancy which terminated one and one-half years previously with a full-term hydrocephalic macerated fetus.

The present pregnancy had progressed normally until shortly before admission to the hospital at the end of the sixth month. Hospitalization was advised because of the absence of fetal heart sounds or fetal movements for six days, sudden enlargement of the abdomen, rapid gain in weight (15 pounds in two weeks), and slight generalized edema. Blood study on admission showed 35 per cent hemoglobin, 2,800,000 red blood count, and 5.0 icterus index.

On the day following admission at 3 P.M., a transfusion of 1,000 c.c. of blood was given, using two donors. Both donors, as well as the patient, were in Group O (IV Moss). This fact, as well as the compatibility in cross-matching, was later corroborated by four different investigators. Thirty minutes later the patient had a chill, and eight hours later she had an asthmatic type of dyspnea with cyanosis.

Uterine contractions began spontaneously that day. At 3:18 A.M. on the following morning the patient was spontaneously delivered of a macerated fetus which was markedly edematous and had an enlarged abdomen due to ascites. Birth weight was about 4 pounds. The placenta was edematous and two to three times the expected size. Autopsy of the baby showed the characteristic findings of hydrops fetalis.

As soon as daylight appeared marked jaundice was noticed (icterus index 200). The jaundice gradually subsided thereafter.

The patient excreted only 10 c.c. of urine during the twenty-four hours after transfusion. On the succeeding three days, the excretion amounted to 15 c.c., 30 c.c., and 90 c.c., respectively. Some improvement in this respect followed thereafter, but the daily total never exceeded 210 c.c. Blood chemistry showed marked retention of nitrogenous end products.

Notwithstanding, or because of the previous transfusion of 1,000 c.c. of blood, the patient became progressively more anemic. On the tenth day post partum, the hemoglobin was 20 per cent and the red blood count 1,300,000. Another transfusion was therefore considered imperative. A total of only 75 c.c. of donor's blood was given very slowly over a period of one and one-half hours. The patient developed asthmatic dyspnea and died about one hour later, on the tenth day post partum.

Partial autopsy showed marked edema of the lungs, bilateral massive pleural effusion and large white kidneys. The cause of death was stated as being acute hemolytic anemia of undetermined etiology with hemoglobinuric nephrosis, anemia, and uremia. It was thought that the hemolytic process had started shortly before admission, and that the first transfusion had precipitated it into full bloom.

All of the donors for these two cases as well as the husbands of both patients have since been tested and are now known to be Rh positive. Case 2 occurred two years before the Rh factor had been discovered, but in Case 1 there is evidence to indicate that the patient was Rh negative. In addition an atypical agglutinin was found in her blood on the fourth day post partum (Case 1), which we now have reason to believe was the anti-Rh agglutinin.

Within four months of the first case, another patient was observed in consultation (October, 1940). This was the case which crystallized the idea that there is a special danger of transfusion inherent in the mother of an erythroblastic baby. In addition, this was the first case of transfusion accident in a mother of an erythroblastic baby in which the anti-Rh agglutinin was found and identified (Case 3).

CASE 3.—Mrs. R. C., aged 32 years, had had 2 previous pregnancies both of which terminated with death of the baby. The patient stated that in 1934, after three days of labor at term, she was spontaneously delivered of a baby which weighed 6 pounds 4 ounces and lived only two hours. No cause for the death had been given to the patient, and it was assumed that trauma was the most likely cause.

Subsequent examination of the records of this delivery in another hospital revealed that the diagnosis given on the baby's death certificate was purpura hemorrhagica and that the autopsy diagnosis was incomplete expansion of the lungs with generalized edema and ascites. During a review of autopsy protocols four years later, this case was reconsidered and independently diagnosed erythroblastosis fetalis by the same pathologist who had done the original autopsy.

The second pregnancy occurred in 1937 and was terminated at about eight months by the delivery of a macerated hydrocephalic fetus, weighing about 6½ pounds. Fetal movements had been absent for two and one-half weeks. There were no signs of toxemia.

The present pregnancy progressed uneventfully and without any sign of toxemia. Eleven days before term an elective cesarean section was done with the hope of obtaining a living child. The baby weighed 6 pounds 12 ounces and was resuscitated with moderate difficulty. Within a few hours of birth it showed signs of pallor, beginning jaundice, and several fairly large blue areas in the skin. A blood count showed hemoglobin 36 per cent; red blood count 1,600,000; total nucleated cells (leucocytes plus nucleated red blood cells) 62,300; with 39 per cent polymorphonuclears, 37 per cent "lymphoblasts," and "many" nucleated red blood cells. The baby became progressively worse and died twelve hours after birth in spite of a blood transfusion of 50 c.c. from the father, given about six hours after birth. Autopsy showed areas of extramedullary hematopoiesis in the liver, spleen, and kidneys. Diagnosis: erythroblastosis fetalis.

Because of a considerable blood loss at the time of operation, a 500 c.c. blood transfusion was given at the close of the operation, using the husband as a donor. There was no chill or other obvious evidence of reaction after this first transfusion. During the immediate postoperative interval, the patient continued to bleed more than usual and her pulse was rapid and weak. On the first day postoperative the hemoglobin was 45 per cent and the red blood count 2,300,000. Therefore, the second transfusion of 500 c.c. was given on the afternoon of the first day, again using the husband's blood. There was no immediate sign of reaction, but one hour later there followed a severe pain in the abdomen and a shaking chill lasting thirty minutes.

Oliguria had already set in, the patient secreting only 200 c.c. during the first thirty-six hours postoperative. On the next four days the total urinary output was 30 c.c., 25 c.c., 45 c.c., and 60 c.c., respectively. The retention of nitrogenous end products was well advanced as early as the third day postoperative when the nonprotein nitrogen was 120. This reached a maximum on the sixteenth day when the nonprotein nitrogen was 350.

The danger of further transfusion was well appreciated. However, the need seemed great (hemoglobin 33 per cent; red blood count 1,240,000 on the second day), and it was thought that a compatible donor was available after careful selection by Dr. Levine. Therefore, 250 c.c. of blood was given on the fourth day. This likewise was followed in one hour by a severe chill.*

*The explanation for the use of this supposedly compatible but actually incompatible blood will be given in a later publication by Levine and Burnham.

In the meantime efforts to obtain large amounts of pooled plasma were finally successful. Starting on the fourth day the patient received 6,150 c.c. of plasma (already diluted half and half with physiologic salt solution) during six days until the patient's plasma protein determinations reached the normal level. This was supplemented with large doses of molar sodium lactate and concentrated glucose in distilled water until the marked acidosis was corrected. It seems very likely that the patient's ultimate recovery can be attributed in large part to the use of the plasma which gave the patient large amounts of the essential fluid constituents of the blood even though the cellular elements were lacking.

The patient's condition was such that she was able to withstand a unilateral parotitis (onset eighth day) and a bilateral bronchopneumonia (onset ninth day) in addition to the marked uremia; albeit for several days the margin seemed very slim.

The hoped-for improvement in urinary output began on the eleventh day when 250 c.c. were excreted. This was followed on succeeding days by 500 c.c., 865 c.c., 1,375 c.c., 1,870 c.c., 3,100 c.c., and 4,425 c.c. The latter two days and the following four days were the only ones on which the urinary output exceeded the fluid intake, and during these six days the moderate peripheral edema largely subsided.

During the course of the case, blood studies were being constantly carried on. The patient was found to be Rh negative, and the baby, the husband, and the first three transfusion donors were Rh positive. The anti-Rh agglutinin responsible for the destruction of donor's blood was first demonstrated in the patient's serum on the eighth day. On the twelfth day the first Rh negative donor was used (500 c.c. in two divided doses) without a reaction of any kind. Another 500 c.c. of slightly incompatible blood was given on the fifteenth day and followed by a chill.* Two days later the patient was still very anemic (hemoglobin 34 per cent; red blood count 1,580,000). Thereafter three transfusions, each of 500 c.c. of Rh negative blood, were given on the eighteenth, twentieth, and twenty-third days, respectively, without any reaction. The patient was now recovering rapidly after having regained consciousness on the twentieth day. She was discharged from the hospital, strong enough to walk a few steps, on the thirty-sixth day.

The following case occurred about one month after Case 3.

CASE 4.—Mrs. E. F. W., aged 38 years, had one spontaneous abortion at eight to nine weeks in 1937, two laparotomies for sterility (one for uterine suspension and appendectomy and one for adhesions), and one previous cesarean section. The second pregnancy had been terminated in 1938 by cesarean section because of a male pelvis with a brow presentation in an elderly primipara. At that time the uterus failed to contract well and the patient was transfused immediately after the operation with 600 c.c. of her husband's blood without any reaction. The baby weighed 8 pounds 3 ounces and had no jaundice or other sign of erythroblastosis.

During the present pregnancy there was some edema of the face and feet, but no other sign of toxemia (weight gain 18 pounds, highest blood pressure 128/84, and no albuminuria). A secondary anemia was present which improved under iron therapy (hemoglobin 65 per cent rose to 80 per cent).

A second cesarean section was done (Nov. 30, 1940), the uterus again failed to contract well and a transfusion of 500 c.c. was given immediately after the operation, again using the husband as a donor. There was no immediate reaction and in fact none for the first three days postoperative. However, on the fourth day, oliguria set in, the urinary output being only 300 c.c. On the following 4 days it was 270 c.c., 510 c.c., 420 c.c., and 180 c.c., but marked improvement began thereafter. On the seventh day there was a considerable nitrogen retention (blood urea nitrogen 81.5) and other signs of uremia. The patient made a gradual recovery, the blood chemistry returning to normal on the twenty-third day.

*See footnote on page 392.

The baby (9 pounds 1 ounce) was pale at birth, had small petechial areas and larger bluish areas in the skin, and breathed very poorly. The blood count on the day of birth showed hemoglobin 40 per cent; red blood count 1,590,000; nucleated cells (white blood cells plus nucleated red blood cells) 198,000; polymorphonuclears 16 per cent, lymphocytes 5 per cent, megaloblasts 4 per cent, and normoblasts 74 per cent. Jaundice appeared twenty-four hours after birth. The baby was given two transfusions and improved rapidly thereafter, receiving 3 transfusions in all. The father's blood was used for all transfusions. The baby was discharged in good condition on the twenty-fourth day.

The anti-Rh agglutinin was found in the mother's blood serum on the sixth day. The mother was Rh negative and the father and baby were Rh positive.

Although the patient in the following case had neither an erythroblastic baby nor a transfusion, it is mentioned because it was the first pregnancy case published in the literature[9] in which the atypical agglutinin was identified as the anti-Rh agglutinin. Moreover, it seems likely that the abortions in the patient's previous history may have been due to the process of immunization. The explanation for the apparent lack of injury to the fetus in the last pregnancy, June, 1940, is not evident. What the effect of the many injections of progesterone might have been upon this is no more than conjecture.

CASE 5.—Mrs. H. H., aged 33 years, had had five previous pregnancies, in only one of which was the outcome satisfactory. In 1928 the first pregnancy terminated with a difficult forceps delivery resulting in intracranial injury, spastic paraplegia, and institutionalization of the child. Two years later a normal child was born by forceps delivery of a face presentation. There followed 2 spontaneous abortions in 1936 at six weeks and three months, respectively, and in 1938 at four and one-half months a third spontaneous abortion (fetus said to have been dead about one day).

The patient was most anxious to have another baby and presented herself before conception for examination and advice. The pregnancy occurred directly and continued to term. In the hope of avoiding abortion, she was given bi-weekly injections of progesterone from the fifth to the thirty-second week of pregnancy, totaling 44 injections almost all of which were of 5 mg. strength. Because the basal metabolism was normal, no thyroid extract was given. The diet was supplemented with extra-vitamins (no vitamin E however) and with adequate doses of iron.

On June 23, 1940, after three days of mild, irregular contractions at term and in the presence of a frank breech presentation with an unchanging, uneffaced cervix, a low flap cesarean section was done. The baby weighed 7 pounds 2½ ounces and showed no sign of erythroblastosis, although a blood count soon after birth was not done.

Preliminary blood examination had shown that both the patient and her husband were in Group A, but that the cross-matching was definitely incompatible. Since this occurred at the same time that Case 1 was under observation, specimens of their bloods were sent for further study. This revealed in the patient's serum the presence of an atypical agglutinin and identified it as the anti-Rh agglutinin.[9] The patient was later found to be Rh negative, and her husband and baby Rh positive. Fortunately a transfusion was not needed. The mother and baby were discharged from the hospital in good condition on the fourteenth day postoperative.

DISCUSSION

The incidence of erythroblastosis has been given as one in every 2,000 confinements. This includes the three accepted clinical forms, namely hydrops fetalis, icterus gravis, and congenital anemia of the newborn. In recent years it has been realized that the disease is more frequent than was formerly thought. Thus Wolfe and Neigus[10] reported an

TABLE I. RÉSUMÉ OF CASES

CASE	AGE	GRAVIDITY	LIVING CHILDREN	Rh	ANTI-Rh AGGLUT.	Rh HUSBAND	Rh BABY	BABY OUTCOME	REMARKS
G. B.	32	iv	1	Neg.	Present	Pos.	?	Macerated fetus, erythroblastosis ?	4 transfusions Rh pos. blood, jaundice, anuria, uremia, death ninth day
J. B.	30	ii	0	?	?	Pos.	?	Macerated fetus, erythroblastosis	1 transfusion 1,000 c.c. Rh pos. blood, jaundice, anuria, second transfusion 75 c.c. Rh pos. blood 1 hr. before death tenth day
R. C.	32	iii	0	Neg.	Present	Pos.	Pos.	Lived 12 hr., erythroblastosis	3 transfusions Rh pos. blood, reaction, anuria, uremia. Recovery after 6,150 c.c. plasma and 1,500 c.c. Rh neg. blood
E. F. W.	38	iii	1	Neg.	Present	Pos.	Pos.	Erythroblastosis, recovery after 3 transfusions	1 transfusion Rh pos. blood, delayed oliguria, uremia. Recovery
H. H.	33	vi	2 (one spastic paraplegia)	Neg.	Present	Pos.	Pos.	Normal baby	Incompatible cross-matching between patient and husband, no transfusion

incidence of 1 in 568, and Javert[11] has found it to be 1 in 400. In the last 1,400 deliveries at the Englewood Hospital we have had 8 cases, an incidence of 1 in less than 200. This is a small series and probably represents a selected sample. However it should be noted that 6 of these 8 cases would have been missed had we not been on the lookout for them, and had not our suspicion been confirmed by the blood studies of Dr. Levine. Of the 6, 2 would have been considered fetal deaths in utero of unknown cause (macerated fetuses), and the remaining 4 would have been considered idiopathic anemias of the newborn, inasmuch as blood smears were made too late to show erythroblasts, and all 4 recovered after transfusions.

Thus it is apparent that the erythroblastosis group must be broadened to include some of the macerated fetuses not due to syphilis, diabetes, or toxemia, and also many if not most of the anemias of the newborn. Some cases of miscarriage likewise belong in the group.

The danger of transfusion for the mother of a baby with erythroblastosis becomes evident. We formerly thought of transfusion accidents only in terms of faulty grouping. The statement has even been made that cross-matching of donor and recipient's blood was unnecessary if one were certain of using the same blood group. But reactions between bloods of the same group have been reported with increasing frequency.[12] This is because the Rh factor and the anti-Rh agglutinin react within the same blood groups, since they are unrelated to the blood groups. When the anti-Rh agglutinin is present, cross-matching in the usual manner often fails to reveal the existing incompatibility. In another case (J. L.[7]), cross-matching between the patient and her husband was carefully done by two commonly accepted methods without detecting any incompatibility, even though it was known to be present.

In the series of 8 cases mentioned before, 2 of the patients were transfused with blood from the same group, and each suffered a fatal or near fatal reaction. Of the 6 other cases, 3 were found to have developed the anti-Rh agglutinin in their blood and likewise would very probably have had severe reactions if transfused. Two of the remaining 3 cases were investigated so long after delivery (six and twelve months, respectively) that the agglutinin might well have disappeared from the blood stream. This leaves only one of the 8 cases in which the danger of transfusion was no more than potential.

Probably the most important aspect of these morbid states is their prophylaxis. In erythroblastosis, we know nothing of the circumstances which permit the immunization of an occasional Rh negative mother by an Rh positive baby and not the immunization of the vast majority of such mothers. Nor can we explain why in the case of H. H., the anti-Rh agglutinin was formed in the mother but caused no apparent harm in the baby. Therefore the prevention of erythroblastosis is still unsolved. Fortunately many of the babies live long enough to be cured by transfusion, provided they are recognized in time.

On the other hand much can be done to prevent a transfusion accident in the mothers with its almost 50 per cent mortality. It is believed that almost all if not all of these reactions can be prevented by a modified cross-matching technique devised by Levine.[6] This consists of the incu-

bation of the mixture of donor's cells and recipient's serum at body temperature for thirty minutes. The mixture is then centrifuged and read as in the usual Landsteiner method. There is no reason why this modification cannot be easily performed in any laboratory. The time element involved (thirty minutes) is no more than is usual with some other techniques. It is usually safer to delay the transfusion thirty minutes than run the risk of an irreversible hemolytic reaction.

Should a mother of a possible erythroblastosis baby require a transfusion, it is safer to determine the Rh status of the mother and use a corresponding donor as already pointed out. Usually this will be an Rh negative donor. Should none of these precautionary measures be available in a given suspicious case, it is safer to use blood substitutes, preferably blood plasma.

CONCLUSIONS

1. Erythroblastosis fetalis is due to the destruction of the baby's blood by the *anti-Rh agglutinin,* which has been formed in the mother's blood by immunization of an Rh negative mother by an Rh positive baby.

2. Severe transfusion accidents in the mothers of erythroblastic babies are exceedingly common and likewise are due to the destruction of the donor's blood by the anti-Rh agglutinin.

3. These reactions are almost always if not always preventable, by means of a modified cross-matching technique.

4. The mothers of erythroblastic babies may be safely transfused preferably after determination of their Rh status, and usually by the use of Rh negative blood.

5. Erythroblastosis is more common than generally appreciated.

6. The group includes cases other than the three accepted clinical forms of hydrops fetalis, icterus gravis, and congenital anemia of the newborn.

7. Early blood counts of supicious babies (early jaundice and/or anemia) will permit the saving of many babies by transfusion.

The author is indebted to Drs. R. L. Barrett, J. G. Gershman, J. W. Prather, and H. W. Taylor for the privilege of presenting their cases.

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229 Engle Street

PARENTERAL VITAMIN K THERAPY IN ANTE-PARTUM WOMEN AND ITS EFFECTS ON THE INFANTS' PROTHROMBIN LEVELS

A Preliminary Report

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MOST of the experimental work done thus far on vitamin K therapy in obstetrics and pediatrics has concerned the oral use of vitamin K in women not in labor and in infants after delivery. In the series of cases described in this report, we have sought to determine the effectiveness, particularly in infants, of parenteral vitamin K therapy administered to pregnant women before the onset of, and during, labor. Our objectives were to determine:

1. Whether parenteral vitamin K therapy affects the prothrombin level of the blood of pregnant women; and whether such therapy influences the prothrombin levels of newborn infants immediately postpartum, and during the first few days of life.

2. The optimum time of administration in the period preceding delivery; and the effective dose of the preparation used.

Vitamin K therapy was applied in the form of 2-methyl-1, 4-dihydroxynaphthalene diphosphoric acid ester tetrasodium $(C_{14}H_{12}O_8P_2Na_4 \cdot 6H_2O)$ "882" salts,* hereafter referred to as Preparation N-123. The antihemorrhagic activity of this preparation has been reported by Foster and Lee and others.[1, 2] It was found to be about 50 per cent more potent than methyl naphthoquinone. Toxicity studies of this preparation in animals[3] show no harmful effects with doses much larger than the therapeutic dose. This vitamin K-like principle is a clear water-soluble preparation. It may be administered orally, subcutaneously, intramuscularly, or intravenously. In our study, the drug was injected intramuscularly in doses of 10 mg. or larger. No local or systemic by-effects or untoward reactions were noted.

METHODS

The blood prothrombin levels were determined in 4 pregnant women (Group I) by the plasma method of Quick,[4] a two-stage method. All other prothrombin de-

*A synthetic substance prepared by Hoffmann-LaRoche, Inc., Nutley, N. J., who kindly provided the necessary supplies for this study in 1 c.c. ampoules of an aqueous solution, 10 mg. each.

terminations were done by the micromethod of Quick,[5] slightly modified as follows:

Five-hundredth cubic centimeter of a thromboplastin solution* was measured from a small carefully graduated pipette into a clean 10 by 70 mm. test tube at room temperature; 0.05 c.c. of blood freshly drawn from a finger or heel puncture was added, and the tube was gently agitated to insure mixing. The time required for clot formation was noted on a stopwatch. This was taken as the blood prothrombin time. Duplicate determinations were run on each case, and invariably they checked within two seconds.

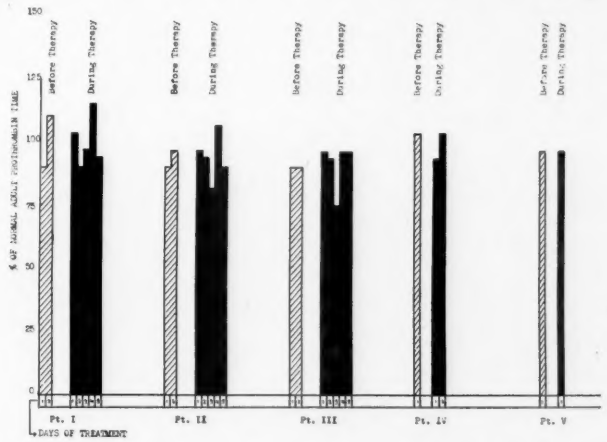

Fig. 1.—Prothrombin levels of ante-partum women receiving parenteral vitamin K therapy several days before labor. Ten milligrams of Preparation N-123 daily by intramuscular injection.

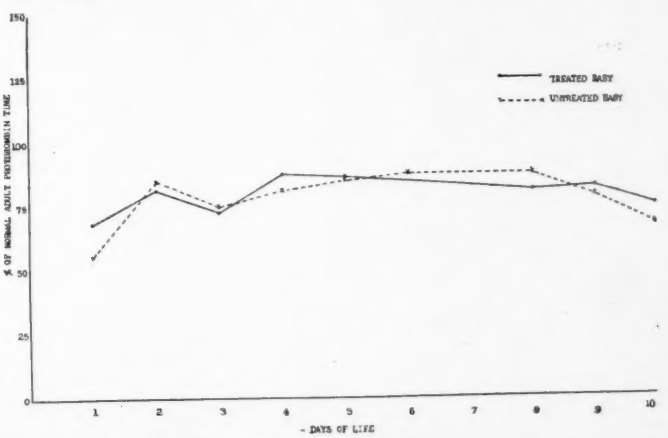

Fig. 2.—Characteristic curve: Prothrombin level of infant born to Patient 1, Group I, who received 6 daily doses, 10 mg. each, of Preparation N-123. Last dose: one week before delivery. No definite effect.

The prothrombin time of the ante-partum women, expressed in percentages of the prothrombin time of normal adult controls, were determined before and after injections of Preparation N-123 (Fig. 1). In the infants, the prothrombin determinations were made as nearly as possible at the same time of day throughout the tests. For control purposes, the same determinations were made, (1) in infants born approximately at the same time but of untreated mothers; and (2) in normal adults, usually post-partum women in the ward.

*Thromboplastin solution was prepared from powdered rabbit brain (thrombokinase) furnished in ampoules by Difco Company.

Our experimental group comprised 27 normal pregnant women chosen at random from the prenatal clinic. The majority delivered spontaneously or were delivered by low forceps. They were divided into five groups as follows:

Group I: 5 ante-partum women. Vitamin K therapy was instituted as near the estimated date of confinement as possible. Ten milligrams of N-123 were given by intramuscular injection daily for six days in three cases; for three days in one case (Pt. 4); and for two days in one case (Pt. 5). Prothrombin determinations were made before administration of the drug, and daily during its use.

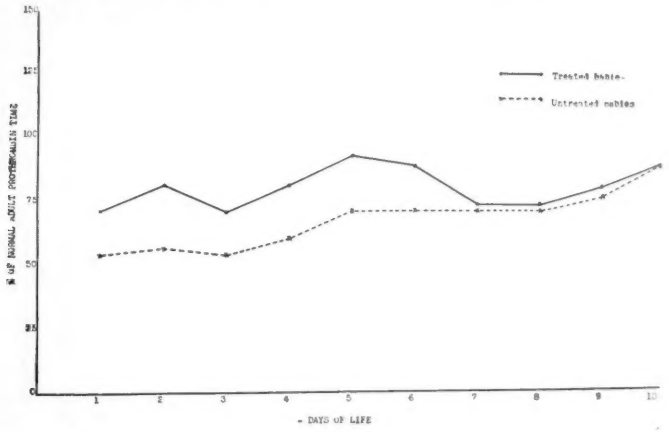

Fig. 3.—Composite curve: Prothrombin levels of 4 infants born to mothers receiving a single dose of 10 mg. of Preparation N-123 within one to seven hours before delivery.

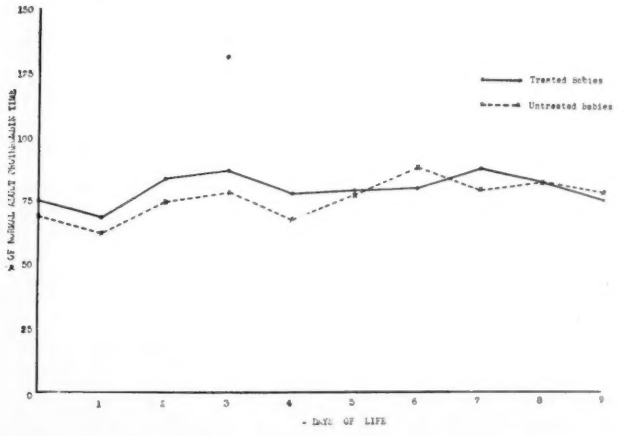

Fig. 4.—Composite curve: Prothrombin levels of 12 infants born to mothers receiving a single dose, 20 mg. of Preparation N-123 by intramuscular injection within twenty minutes to twenty-one hours before delivery (includes determination in 3 infants whose prothombin levels were not affected). The effect, evident at birth, wears off at about the fifth day.

1. The pre-injection prothrombin levels were within normal limits in the mothers in this group; and, as was to be expected, administration of the drug did not significantly change the prothrombin levels (Fig. 1).

2. The prothrombin levels of the infants born of these mothers who had received injections of vitamin K terminated several days before delivery (from two to twelve days) showed no definite elevation compared with control infants born of

untreated mothers. Fig. 2 illustrates a typical case where the maternal administration of the drug was terminated one week before delivery occurred.

In view of the results observed in Group I, it was decided to administer the vitamin K-like principle to women in labor, and to study the effects on the infant prothrombin level when the dosage was increased and the time interval before delivery was reduced.

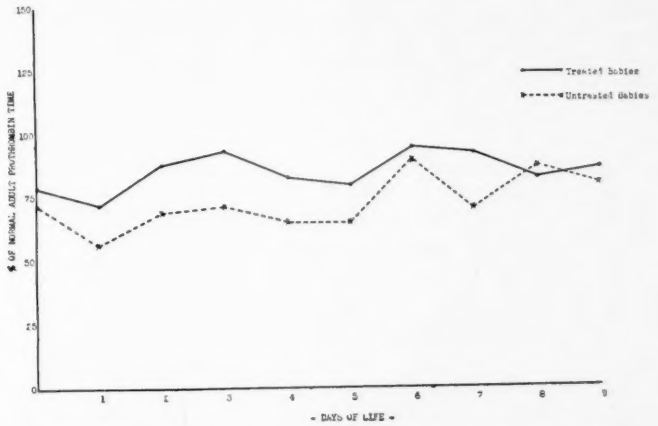

Fig. 5.—Composite curve: Prothrombin levels of 9 infants born to mothers receiving a single dose, 20 mg. of Preparation N-123 by intramuscular injection within twenty minutes to twenty-one hours before delivery.

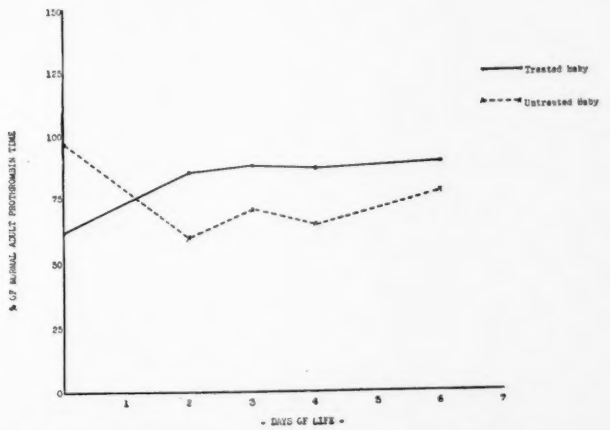

Fig. 6.—Single case, Group III. Prothrombin level of infant born to mother receiving a single dose, 20 mg. of Preparation N-123 by intramuscular injection twenty minutes before delivery illustrates rapid absorption from maternal circulation.

Group II: 4 ante-partum women. Vitamin K therapy was instituted during labor. A single dose of 10 mg. of N-123 was injected intramuscularly one hour before delivery in one case, six hours before in one case, and seven hours before in two cases.

The prothrombin levels of infants born of these mothers were significantly changed compared with infants born of untreated mothers. In Fig. 3, the results are averaged, and it will be noted that there is about a twenty per cent increase in the prothrombin levels of the treated infants the first day of life, and that this effect is maintained for about six days.

Group III: 12 ante-partum women. In these cases, we sought to determine if there was any greater effect obtained by increasing the dose of vitamin K. A single injection of 20 mg. of Preparation N-123, was given intramuscularly within twenty minutes to twenty-one hours before delivery.

The prothrombin levels of 75 per cent of the infants born of these mothers (9 cases) were definitely elevated, and 25 per cent (3 cases) showed no changes. Figs. 4 and 5 show the curves averaged from these cases, and it will be noted that they resemble the curves in Group II. We have no explanation to present for the lack of effect observed in 3 cases.

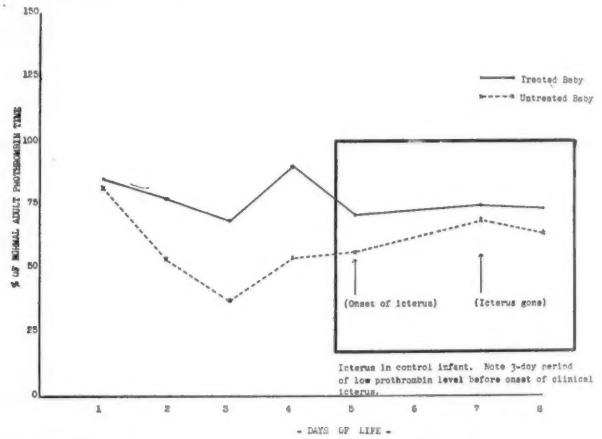
Treated Baby
Untreated Baby
(Onset of icterus)
(Icterus gone)
Icterus in control infant. Note 3-day period of low prothrombin level before onset of clinical icterus.
- DAYS OF LIFE -

Fig. 7.—Single case, Group IV. Prothrombin level of infant born to mother receiving a single dose, 30 mg. of Preparation N-123 by intramuscular injection one and one-half hours before delivery.

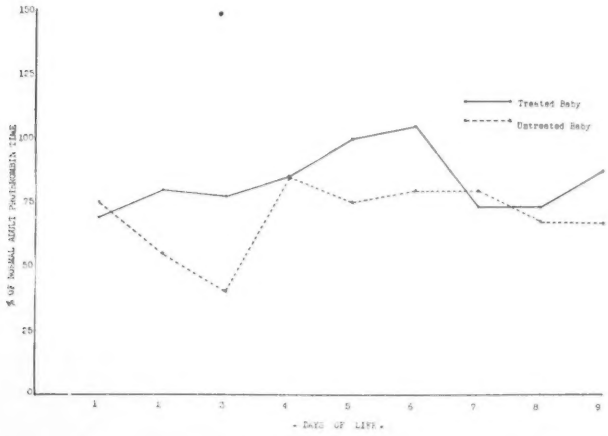

Fig. 8.—Prothombin level of infant born to mother receiving two doses, 10 mg. each, of Preparation N-123 by intramuscular injection. First dose, twenty-three hours before delivery; second dose, eleven hours before delivery.

Group IV: 3 ante-partum women. In two of these cases a single intramuscular injection of 30 mg. of Preparation N-123 was given before delivery. In one case the injection was made one and one-half hours prior to delivery; and in the second case five and one-fourth hours before. The third patient received a larger dose, 40 mg. of N-123, in a single injection four and one-half hours before delivery.

1. The prothrombin levels of the two infants born of the mothers receiving the 30 mg. doses were definitely elevated; in the single case receiving 40 mg. no effect was noted.

2. The results in these cases where larger doses of vitamin K (20, 30, and 40 mg.) were used showed no greater elevation of the infants' prothrombin levels than the cases in Group II where 10 mg. doses were employed.

3. The effectiveness of parenteral administration of this vitamin K principle in regard to time intervals before delivery is shown in Fig. 6. This shows elevation of the prothrombin level in a case where the drug was injected only twenty minutes before birth of the baby. The drug seems less effective if more than about 15 hours have elapsed between the time of injection and delivery.

4. The curve of one of the patients in Group IV who received 30 mg. of N-123 one and one-half hours before delivery is shown in Fig. 7. Definite effect is evident in the treated case, and it is also of interest to note in the control infant, who developed clinical physiologic jaundice of the newborn, that the extremely low blood prothrombin level antedated the icterus by two days.

Group V: 3 ante-partum women. These patients all had prolonged labors, one case being terminated by a midforceps delivery. In two cases, a 10 mg. dose of N-123 was given early in labor and repeated once in each case about ten hours later. The third case, which was the instrumental delivery, received 3 injections of 10 mg. each of the drug at twelve hourly intervals during a fifty-hour labor, and delivered twelve hours after the last injection.

One case (Fig. 8) showed definite elevation of the prothrombin level of the baby born of the treated mother. The second case, although the last dose of the drug was given only three hours before delivery, showed only slight prothrombin level elevation, and the case in which midforceps was employed showed no effect. At present we have no explanation for the lack of action in these two cases.

SUMMARY

1. Parenteral vitamin K therapy does not seem to affect the normal prothrombin level in pregnant women.

2. If a course of parenteral vitamin K therapy is terminated several days before delivery, the prothrombin level of the infant is not affected.

3. Parenteral vitamin K therapy given during labor caused definite elevation of the blood prothrombin level in 16 of 22 infants (73 per cent).

4. Use of doses of vitamin K larger than 10 mg. produced no greater elevation of the prothrombin level.

5. Elevation of the infant's prothrombin level seems to occur very quickly after injection in the mother. If more than fifteen hours elapse between injection of the drug and delivery, the effect seems to be decreased.

CONCLUSIONS

In this study a new water-soluble vitamin K-like principle has been administered parenterally to ante-partum women, and its effect on the prothrombin levels of the infants has been determined.

The drug apparently does not alter the normal prothrombin level of the mother, but its effects in the infant seem to be manifested promptly after injection. Therefore we may assume placental transmission of this substance occurs.

If delivery does not occur within a few hours after injection, the effect is less; the substance is probably destroyed or excreted by the maternal system. It would seem advisable therefore to repeat the injection shortly before delivery.

It is generally admitted that intracranial hemorrhage in infants probably occurs before or during delivery. If it is possible to elevate the infant's prothrombin level in utero by administering vitamin K to the mother in a rapidly absorbable form, this should be more effectual than treating the infant after delivery.

(Further studies are being made with Preparation N-123 in an endeavor to observe its effects on the prothrombin levels when injected in infants immediately after birth.)

We wish to express our appreciation to Dr. Adolph Bernhard for his modification of the Quick microprothrombin method as described in this paper.

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VITAMIN A IN PREGNANCY*

II. Comparison of Dark Adaptation and Serum Tests

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THIS is the second of a series of studies to determine the value of fortifying prenatal diet with artificial vitamins as indicated by both subjective and objective tests for vitamin A among clinic pregnancies under better than average dietetic management.

Vitamin A was selected for several reasons: (1) Relatively practical tests; (2) clinical manifestations of deficiency due to keratinizing epithelial metaplasia of the alimentary (glossitis, parotitis, etc.), respiratory (tracheobronchitis), urinary (pyelocystitis), ocular (xerophthalmia and cutaneous (keratosis pilaris) systems; (3) possible relation to liver dysfunction (pre-eclampsia) due to liver storage, and to puerperal morbidity due to epithelial change.

The studies are based on the assumption of general population deficiency of vitamin A intake according to the complete report of Lehman and Rapaport[1] who reviewed clinical manifestations of deficiency among soldiers, prisoners, and asylum inmates, as well as among medical students, and also dietetic deficiency among 66 per cent of 4,000 working

*Read at a meeting of the Obstetrical Society of Philadelphia, March 6, 1941.

families as reported by the U. S. Labor Bureau. Holman[2] likewise found 26 per cent of 38 patients admitted to the Stanford-Lane clinic for medical-surgical care markedly deficient according to the Hecht Adaptometer, and called attention to the vital necessity of vitamin A saturation to prevent postoperative infections (parotitis, bronchitis, pneumonia, and pyelocystitis). Williams and others[3] also recently found dietetic A deficiency in 62 per cent of 123 pregnant clinic women, with 37.5 per cent abnormal dark adaptation without correlation.

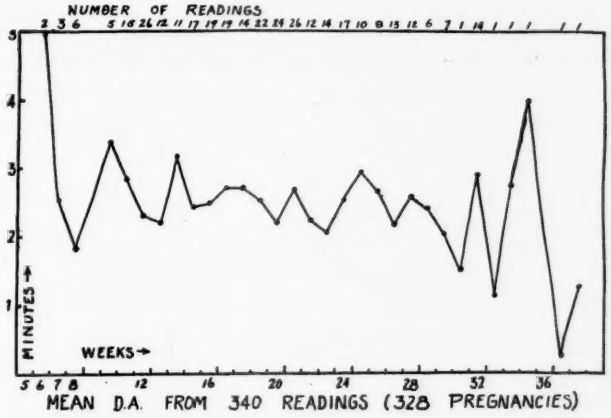

Fig. 1.—Normal adaptometer averages among pregnant women under good conditions.

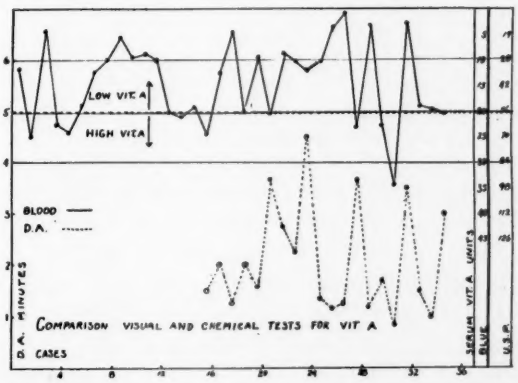

Fig. 2.—Extremely variable blood vitamin A (upper) of 35 pregnancies, compared with normal adaptometer readings (lower). Fifty additional blood tests also showed excessive variations.

Our prior observations[4] from 880 adaptometer tests among 200 pregnancies under good prenatal care showed much less deficiency than generally reported, i.e., 9 per cent gross, 3 per cent corrected, and 4 per cent borderline cases. Since 6 per cent gave an initial false-positive deficiency test, subsequently normal, we stressed the necessity of repeating all abnormal readings and assumed either that the accuracy of the method was questionable or that increased appetite and improved diet of our patients resulted in scant vitamin A deficiency in pregnancy.

To determine the above question, we present a second study in two parts: (1) Mostly single, corrected, dark adaptation tests of 328 clinic pregnancies under precisely the same conditions as before; (2) a small series of 34 pregnancies tested for blood serum vitamin A by the Clausen and McCoord method, as well as by adaptometer.

According to Fig. 1, there is less actual "night blindness" (over five minutes) than in our first series, but generally higher readings due no doubt to mostly single tests. There were only 7 (2.13 per cent) values above five minutes from 340 readings out of 328 patients, but 5 of these were primary false readings, subsequently normal, so that the remaining 2 consistently high cases represent but 0.62 per cent abnormals. Of these 2, 1 was entirely uncomplicated, and 1 showed only pre-eclampsia, whereas there were 23 instances of toxemia among the remainder, among whom there were also 6 cases of anemia with hemoglobin below 60 per cent (Dare). There were no other significant complications in this group, except one case of cutaneous papillary keratosis.

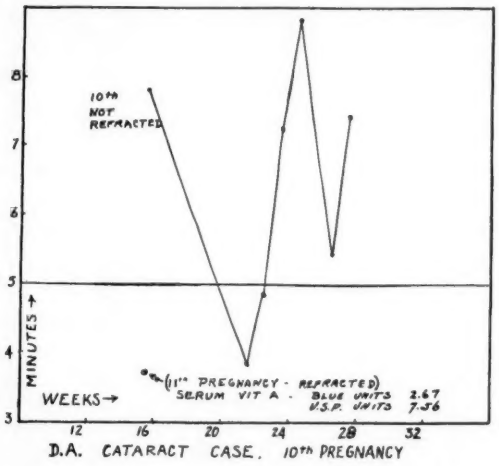

Fig. 3.—False high adaptometer readings in tenth pregnancy due to eyestrain. Normal reading in eleventh pregnancy (lower) with vision corrected, but false blood test for vitamin A.

Fig. 2 shows the results of blood serum tests for vitamin A according to the method of Clausen and McCoord.[5] This test is a fairly complicated colorimeter differentiation between petroleum ether extraction from serum of 15 c.c. of blood, of carotinoids and vitamin A by potassium dichromate and antimony trichloride, respectively. The amount of vitamin A is calculated as arbitrary (blue) units, representing 2.8 U.S.P. units per 100 c.c., allowing considerable deviation.

Our single calculations showed excessively wide excursions due to lack of experience as well as to difficulty with carotinoid yellow in the colorimeter, but if accepted as a relative test, indicate frequent (40 per cent) deficiency with no correlation whatever to the adaptometer readings.

For evaluation, the clinical applications of Clausen and McCoord are important, from study of newborns, infants under six months, six to twenty-four months, and over two years, from which they found a fall of serum vitamin A due to fever proportionate to that due to low carotene diet. They found high blood carotene in normal, diabetic and hypothyroid subjects with xanthosis cutis, but similar

levels without those skin lesions in nephrosis and chronic nephritis, and in the last instance, high vitamin A level indicating possible loss of liver storage. The placenta appears to be no barrier to carotene, and probably not to vitamin A.

Steininger, Roberts, and Brenner[6] from Chicago University have established long range adult levels from 4 subjects and one control after prolonged depletion laboratory diets, and normal single values among 34 average subjects one-half supplemented with vitamin A and one-half unsupplemented, taking fasting blood samples. They found no correlation between biophotometer and blood tests for vitamin A, but direct relation to depletion diet and supplementary feeding by serum estimations.

Depletion diets caused a maximum drop from 17 to 7.1 blue units, and lowest level in any case, 5 blue units. A mean of 9.4 blue units per 100 c.c. of serum with an average deviation of 2.6 units among 17 unsupplemented average adults and a mean of 15.8 blue units per 100 c.c. with an average deviation of 3.0 units in supplemented cases was established.

Fig. 3 represents severe consistent "night blindness" in one woman during a tenth pregnancy, complicated by long-standing unrefracted cataract in one eye plus pre-eclampsia, as compared to normal dark adaptation during her uncomplicated eleventh pregnancy with corrective glasses. This case demonstrates error in dark adaptation by local ocular pathology, since the toxemia was mild.

SUMMARY AND CONCLUSIONS

1. Three hundred and twenty-eight additional pregnant women under good prenatal dietetic management were tested by the Feldman adaptometer for deficient vitamin A; and 34 were tested similarly and by blood serum estimations.

2. The adaptometer indicated only 0.62 per cent deficient in vitamin A, whereas the serum content was abnormal in 40 per cent of single readings as well as uncorrelated.

3. Subjective biophotometric tests for vitamin A are not applicable for determination of the status in pregnancy.

4. Chemical tests of pregnancy blood serum also offer doubtful means of assaying vitamin A capacity in pregnancy.

5. Dietetic insufficiency in pregnancy should be assumed, and artificial vitamin A supplement offered in all cases.

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DISCUSSION

DR. PHILIP F. WILLIAMS.—Some months ago a study was made at the Presbyterian and Jewish Hospital Prenatal Clinics of the vitamin A content in the diets of 123 pregnant women. Simultaneously the dark adaptation time was determined. We found that there was a marked deficiency of vitamin A content in the diet of 62 per cent of the women; and a considerable deficiency in the dark adaptation time of 37½ per cent. We did not find, however, that there was a close relationship between the process of regaining vision in darkness and the intake of vitamin A in the diet.

We considered our series too small to draw conclusions with reference to subnormal vitamin A intake and febrile morbidity in the puerperium. It has been noted, however, in Wales that the distribution of accessory foodstuffs to indigent pregnant women in the Rhonda Valley bringing their vitamin A intake to above normal was followed by a much lower incidence of sepsis, than in comparable untreated series.

In our study we did not have access to a physiologic chemist, and we were unable to add a study of the blood content of vitamin A. Very recently, however, Pett and LePage and Steininger, Roberts and Brenner have correlated in two studies the diet content of vitamin A, dark adaptation time, and the blood content of vitamin A. Pett and LePage regard the blood level of vitamin A as a variable, dependent on the absorption and transference of vitamin A in the tissue, and conclude that adaptation time is not sufficiently sensitive to detect these changes. They noted some evidence of diurnal rhythm for vitamin A in the blood. Pett and LePage found that a definite correlation existed between the vitamin A in the blood and vision tests for vitamin A deficiency. On the other hand Steininger and her group in Chicago felt that that amount of vitamin A in the fasting blood is directly affected by the amount of vitamin A in the diet and that the blood level depends upon the previous day's diet as well as upon the habitual intake. They do not feel that the blood level at any given time would necessarily reflect the body stores of the substance. They conclude in contradiction to Pett and LePage that no correlation exists between the vitamin A in blood and the biophotometric readings.

The subject of nutrition in pregnancy is a neglected phase of obstetrics. In our dietary survey of some 550 pregnant women we have found that very few women at any economic level ingested a diet which is regarded as optimum for pregnancy.

If the high proportion of selective service rejections for nutritional deficiencies in the men who have been examined is equalled among the women, we may expect an equally high proportion of unfit women trying to bear children. The disasters in this group undoubtedly have a marked influence on our maternal mortality, stillbirth and neonatal death rates.

DR. ROBERT SHOEMAKER.—Our work indicates that the adaption test is relatively worthless; certainly there are more than 6 per cent of women low in vitamin A. Likewise we have not done enough blood studies for these to be considered important. Variations are too great, and we know there are many mistakes.

Hellmann, R.: Concerning the Harmlessness of Pantocain for Spinal Anesthesia With Special Reference to the Circulatory Conditions and the Blood—Cerebral Fluid—Relationship, Ztschr. f. Geburtsh. u. Gynäk. **120**: 1, 1939.

Pantocain is particularly suitable for spinal anesthesia in gynecologic operations. With the previously used viscotic pantocain "L" two deaths were encountered. In the second series of 600 cases, there was not a single death even though no prophylactic measures were taken to prevent circulatory collapse. There were no failures and the anesthesia lasted over two hours. The author believes that the changes in the cerebral fluid which have been observed by some investigators are of little significance. No toxic symptoms appeared as a result of the pantocain even when this anesthetic was repeated.

A fall in blood pressure during a spinal anesthesia is an indication of beginning vasomotor collapse. In obstetrics spinal anesthesia is used in carrying out the Delmas procedure. The only collapse in the author's series of 600 cases occurred during a cesarean section.

Headaches do not often occur after pantocain, and there were no serious complications.

J. P. GREENHILL.

PROTHROMBIN CONCENTRATION AND MINERAL OIL*

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(From the Department of Obstetrics and Gynecology, The New York Hospital and Cornell University Medical College)

DURING an investigation of the prothrombin concentration† in normal pregnancy, one patient, having a prothrombin concentration of 100 per cent of normal in the twelfth week of gestation, developed an unexplained decrease to 71 per cent. During the following twenty weeks, synthetic vitamin K (Thyloquinone, Squibb) was administered orally, and the prothrombin level did not increase and ranged between 70 and 80 per cent. It was only after intramuscular injections of vitamin K that the prothrombin was raised to 100 per cent in the thirty-second week of gestation (see Fig. 1). Thereafter, a second decline occurred to 52 per cent, despite the fact that the patient was eating an adequate diet, was gaining weight properly, and was taking vitamin K orally. Finally, close interrogation disclosed the fact that the patient had taken mineral oil at intervals since the thirteenth week of gestation without our knowledge. On discontinuing the oil, and continuing the oral and intramuscular administration of K, the prothrombin level was maintained at 100 per cent up to term, during labor and the puerperium. In this regard, the cord blood prothrombin is of interest, as it was only 33 per cent of normal, which is not a significant increase, despite the large amount of vitamin K given to the mother before and during labor.

Mineral oil is commonly used by many either intermittently, two or three times a week, or regularly at daily intervals; therefore, several patients were studied under both conditions. The results are tabulated in Table I.

As shown in the table, intermittent use of mineral oil reduced the prothrombin levels in 3 out of 9 patients (33 per cent); while daily intake

TABLE I. PROTHROMBIN CONCENTRATION AND MINERAL OIL

CASES	OIL INTERMITTENTLY	PROTHROMBIN CONCENTRATION PER CENT	CASES	OIL DAILY	PROTHROMBIN CONCENTRATION PER CENT
1. O'C.	15 c.c. b.i.w.	100	1. G.	30 c.c. t.i.d.	81
2. S.	15 c.c. t.i.w.	100	2. B.	30 c.c. b.i.d.	69
3. A.	15 c.c. b.i.w.	100	3. D'A.	30 c.c. b.i.d.	23
4. H.	20 c.c. t.i.w.	100	4. G.	15 c.c. b.i.d.	52
5. G.	15 c.c. t.i.w.	100	5. E.	15 c.c. t.i.d.	100
6. A.	30 c.c. t.i.w.	100	6. C.	30 c.c. b.i.d.	100
7. P.	15 c.c. t.i.w.	33	7. S.	30 c.c. t.i.d.	69
8. G.	15 c.c. t.i.w.	69	8. C.	15 c.c. t.i.d.	100
9. C.	15 c.c. t.i.w.	61	9. J.	30 c.c. t.i.d.	33
			10. J.	30 c.c. t.i.d.	61

*Submitted for publication, June 4, 1941.

†The Warner, Brinkhous and Smith technique was used for the Prothrombin determinations under a grant from the John and Mary R. Markle Foundation through the courtesy of Dr. William DeWitt Andrus.

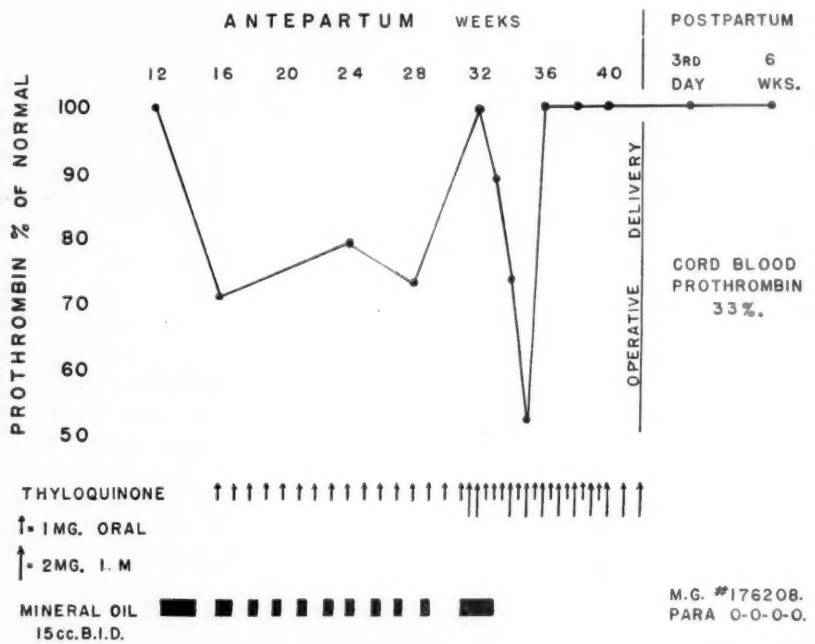

Fig. 1.—The effect of mineral oil on the prothrombin concentration in a patient during pregnancy.

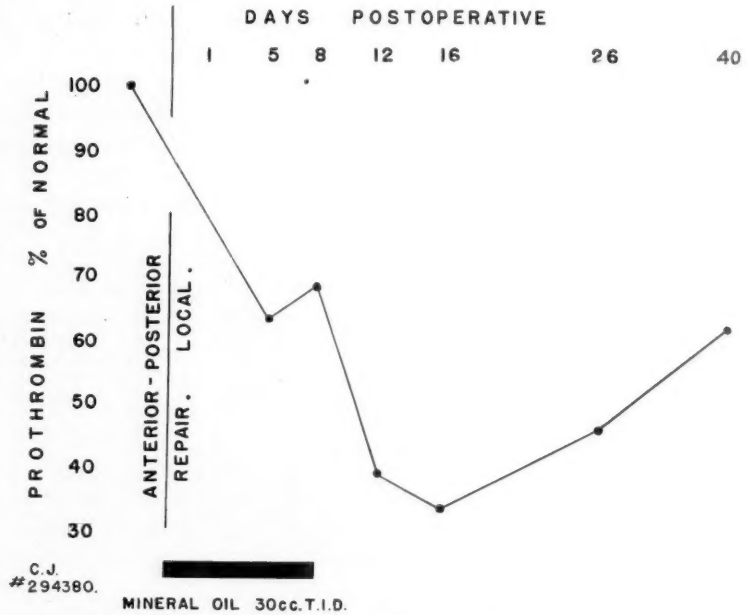

Fig. 2.—Marked lowering of the prothrombin concentration following the use of mineral oil in a patient with a vaginal repair.

of the oil for one or two weeks or longer, resulted in a lowered prothrombin in 7 out of 10 patients (70 per cent). Apparently, mineral oil interferes with absorption by adsorption of vitamin K, or by inhibiting bacterial synthesis in the intestine. The oil may even accumulate in the liver cells. Whatever the mode of action, the evidence suggests the occurrence of hypoprothrombinemia in certain patients following the oral ingestion of mineral oil. In order to prove or disprove this contention, a more systematic study was made on a number of pregnant and nonpregnant individuals.

The prothrombin curve of a gynecologic patient, on whom an anterior and posterior repair was performed, under local anesthesia, is shown in Fig. 2. She was given mineral oil for eight days, with a reduction in the prothrombin level from an initial value of 100 per cent to 68 per cent. A further drop to 33 per cent occurred even after the oil had been discontinued for another eight-day period. Thereafter, a gradual increase occurred without the administration of synthetic vitamin K. This patient had an uncomplicated postoperative course, and an adequate diet was maintained throughout.

An obstetric patient was studied next, since her prothrombin concentration was 33 per cent of normal in the thirty-sixth week of gestation. The administration of thyloquinone orally and parenterally produced a rise to 90 per cent at term. Delivery was spontaneous after a twenty-eight-hour labor, and at this time the prothrombin level was 41 per cent despite the fact that 2 mg. of thyloquinone was given during labor. The prothrombin was 54 per cent on the third post-partum day. At this time, mineral oil was prescribed as shown in Fig. 3, and 1 mg. of thyloquinone was given daily with bile salts. Nevertheless, the prothrombin decreased to a critical level of 23 per cent; therefore, the oil was discontinued. The vitamin K was continued, and ultimately the prothrombin level was 100 per cent. The cord blood prothrombin was 17 per cent of normal despite the administration of vitamin K to the mother, and it appears that if the mother is deficient, she will retain the vitamin K for her own needs and that little reaches the child. Incidentally, this patient also had avitaminosis C, and we have seen such an association in a number of other patients. Fifty milligrams of cevitamic acid were given daily without a satisfactory rise antenatally, indicating that the dosage should have been greater.

The record of a patient with chronic bowel obstruction (following five laparotomies), for which mineral oil has been taken daily, is shown in Fig. 4. The initial prothrombin was 68 per cent of normal, and the intramuscular administration of 4 mg. of thyloquinone produced an elevation to 100 per cent. During this time, it was necessary to continue the mineral oil, and in a week's time, the prothrombin had decreased to its original level. The hypoprothrombinemia was corrected by the parenteral administration of vitamin K, indicating that even if the oil accumulated in the liver, the production of prothrombin is not interfered with. We have observed several other patients with a prothrombin concentration of around 70 per cent of normal when mineral oil had been taken daily over long periods of time.

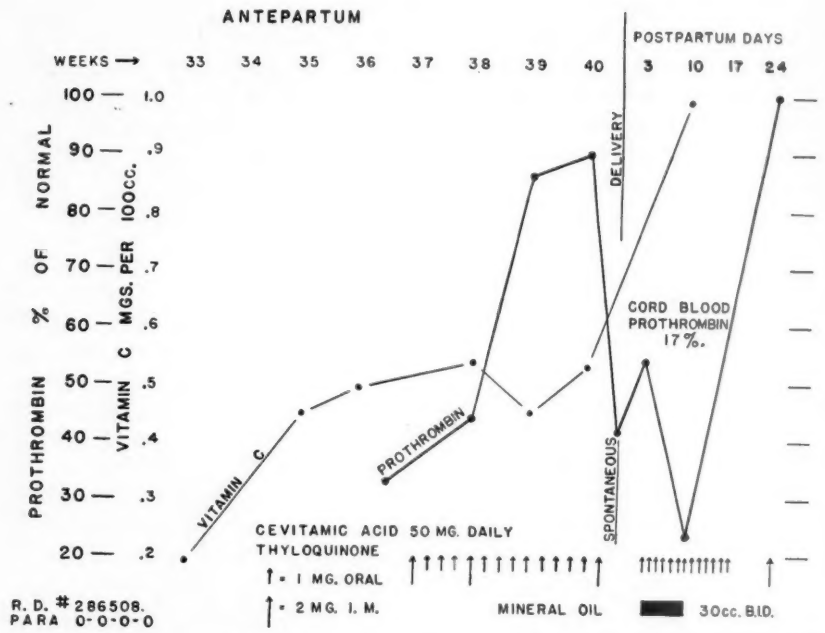

Fig. 3.—Hypoprothrombinemia during pregnancy, corrected by the administration of vitamin K; its recurrence following parturition and further decrease after mineral oil was given daily with vitamin K.

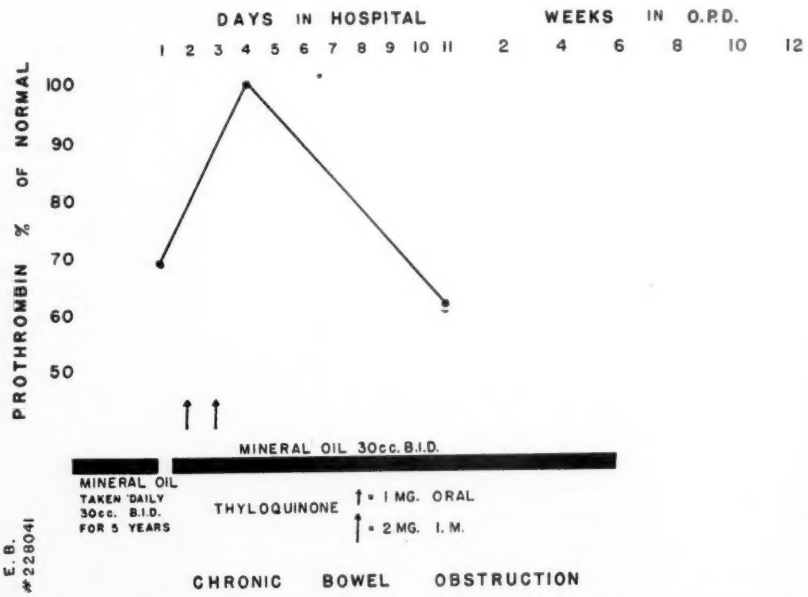
DAYS IN HOSPITAL
WEEKS IN O.P.D.
1 2 3 4 5 6 7 8 9 10 11 2 4 6 8 10 12
PROTHROMBIN % OF NORMAL
100 90 80 70 60 50
MINERAL OIL 30cc. B.I.D.
MINERAL OIL TAKEN DAILY 30cc. B.I.D. FOR 5 YEARS
THYLOQUINONE
↑ = 1 MG. ORAL
↑ = 2 MG. I. M.
E. B. #228041
CHRONIC BOWEL OBSTRUCTION

Fig. 4.—Hypoprothrombinemia in a patient with a chronic bowel obstruction in whom parenteral administration of vitamin K produced a normal prothrombin concentration.

Another patient was seen in the twenty-eighth week of gestation with a prothrombin concentration of 42 per cent of normal. Mineral oil had been taken for years. The prothrombin was increased to 81 per cent by withdrawal of the oil and correcting the diet so that spinach, watercress, and lettuce were included. Of interest is the fact that in 1938 this patient sustained a post-partum hemorrhage for which a transfusion was given. Thyloquinone, 1 mg. daily, was given orally

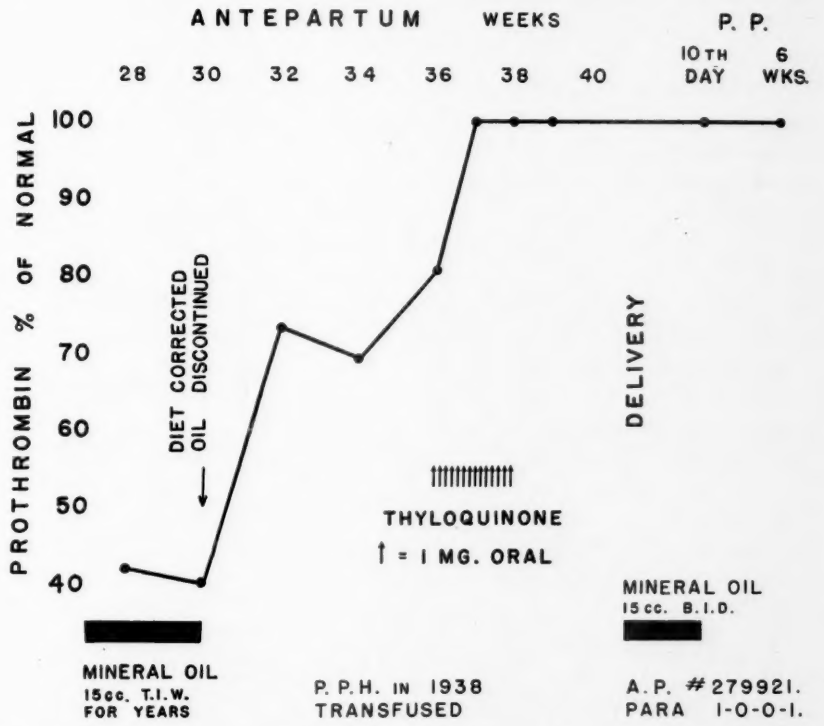

Fig. 5.—Showing an increase in the prothrombin concentration following dietary correction and discontinuance of mineral oil.

for two weeks during which time the prothrombin concentration was maintained at 100 per cent of normal (Fig. 5). Delivery was spontaneous with a blood loss of 200 c.c. Mineral oil, 15 c.c. b.i.d., was given for a short period post partum (ten days) without a drop in the prothrombin concentration. Occasionally, small amounts of oil failed to lower the prothrombin level in patients having had an adequate intake of vitamin K prior to the administration of the oil.

Mineral oil is frequently prescribed for pregnant patients, and since it appears to induce hypoprothrombinemia in certain patients, the routine administration of vitamin K in pregnancy under such circumstances may prove unsuccessful. This is of practical application in the treatment of maternal deficiency as well as in the reduction of the incidence of hemorrhagic disease of the newborn. The oil also interferes with the absorption of carotene, the precursor of vitamin A, according to Rowntree and others. It is possible that it prevents the metabolism

of other fat-soluble vitamins, i.e., D and E. In any event, the use of mineral oil may not be the innocuous habit that its ease in administration has caused it to become.

After our observations had been made, it was learned that Elliott, Isaacs, and Ivy had produced prothrombin deficiency with mineral oil in rats on an adequate diet. They stated that there was insufficient evidence to conclude that oil interfered with absorption of vitamin K. They doubted that the oil produced liver injury.

CONCLUSIONS

1. A lowering of the prothrombin concentration was observed in a patient taking mineral oil without our knowledge, and was responsible for our ultimate discovery of a probable relationship.

2. Oral ingestion of mineral oil in daily doses was associated with lowered prothrombin values in 70 per cent of the patients, while intermittent use of the oil resulted in hypoprothrombinemia in 33 per cent of the cases.

3. The prothrombin concentration in patients receiving oil daily was often reduced to lower levels than when oil was used intermittently.

Occasionally, small doses of oil failed to lower the prothrombin level of patients having had an adequate diet. Whether larger doses will do so awaits further investigation.

4. The role of mineral oil in producing hypoprothrombinemia is probably by prevention of absorption of vitamin K, or by adsorption of the vitamin by the oil, or by interfering with bacterial synthesis. The accumulation of the oil in the liver parenchyma is also probable but does not prevent utilization of vitamin K administered parenterally as shown by one case.

5. From the evidence at hand, the oral administration of vitamin K to pregnant women may prove of little or no value unless the simultaneous use of mineral oil is curtailed.

6. The effect of interdicting the maternal use of mineral oil on the incidence of hemorrhagic disease of the newborn is awaited with interest.

The thyloquinone was supplied by E. R. Squibb & Co.

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PROTHROMBIN CONCENTRATION IN NORMAL PREGNANCY*

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THE prothrombin concentration of blood plasma has been shown repeatedly in the literature to be related to the intake of vitamin K and to proper liver function. There is a paucity of information regarding the maternal prothrombin values although pregnant patients have been studied by many investigators with regard to reduction of the incidence of hemorrhagic disease of the newborn by ante-partum or parturitional administration of vitamin K. A knowledge of the prothrombin concentration in pregnancy is extremely important in order to determine the incidence of vitamin K deficiency and also to verify or refute the rationale of administering vitamin K to every pregnant patient.

In order to clarify this situation somewhat, the prothrombin concentration of 200 normal pregnant women was determined. At times significant variations were observed, but in general, the majority of the patients showed a normal prothrombin concentration indicating adequate intake and utilization of vitamin K.

The Warner, Brinkhous, and Smith technique was used for the prothrombin determinations.† The 200 normal patients were studied at various intervals during the antenatal period and again in labor and in the puerperium. Of the total number, 15 had values determined at monthly intervals, but since no significant variation was observed, all of the data were combined and average values were obtained, and these are presented in Fig. 1. Of importance in interpreting this curve is the fact that 225 of the 400 determinations comprising it were 100 per cent of normal. Of the 200 patients studied, 170, or 85 per cent, showed a concentration between 71 and 100 per cent, and 30, or 15 per cent, were 70 per cent or below. Many in the latter group were given synthetic vitamin K either orally or by intramuscular injection with elevation in the prothrombin values often to 100 per cent and, therefore, were considered to have hypovitaminosis K on a nutritional or metabolic basis in the absence of liver disease.

As shown in Fig. 1, the primary trend of the prothrombin concentration is upward during pregnancy, with the highest value occurring at term. Secondary trends are apparent when the curve is studied from the standpoint of the trimesters of pregnancy. In early pregnancy, the prothrombin concentration is lowest, probably due to a lowered intake of foods containing vitamin K because of "morning sickness" and its attendant nausea and vomiting. Thereafter, the secondary trend is up-

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†These determinations were made possible under a grant from the John and Mary R. Markle Foundation through the courtesy of Dr. William DeWitt Andrus.

ward so that at the beginning of the second trimester of pregnancy, the prothrombin level is 94 per cent of normal. However, a distinct lowering occurs at the end of the second trimester. This may be due to requirements of the fetus. On the other hand, the patients may have been advised to take mineral oil, which the authors have shown elsewhere produces significant lowering of the prothrombin concentration in certain patients. In the last trimester, a gradual increase takes place again, so that at term the average prothrombin level has reached 95 per cent of normal.

At the time of delivery, there is a decrease in the prothrombin concentration, although only 14 per cent of the patients studied at this time were below 70 per cent. These patients would probably have profited by the administration of vitamin K either just prior to, or during, parturition in order to improve their deficiency. The administration of vitamin K under such circumstances would probably not benefit the child since the prothrombin concentration of the cord blood

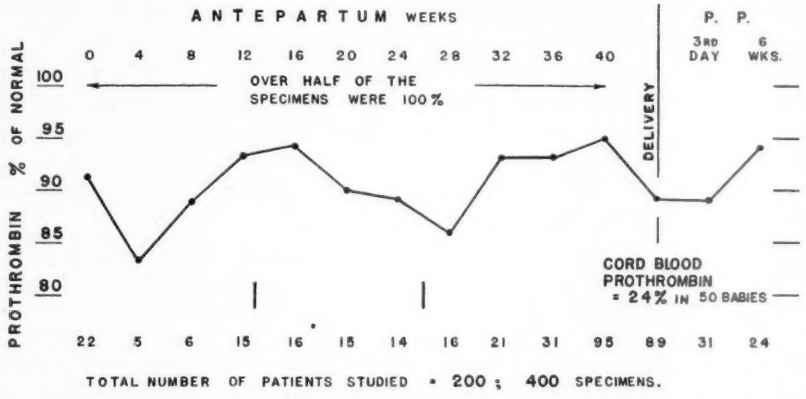
ANTEPARTUM WEEKS
P. P.
3RD DAY
6 WKS.
0 4 8 12 16 20 24 28 32 36 40
PROTHROMBIN % OF NORMAL
100
95
90
85
80
OVER HALF OF THE SPECIMENS WERE 100%
DELIVERY
CORD BLOOD PROTHROMBIN = 24% IN 50 BABIES
22 5 6 15 16 15 14 16 21 31 95 89 31 24
TOTAL NUMBER OF PATIENTS STUDIED • 200 ; 400 SPECIMENS.

Fig. 1.—Plasma prothrombin concentration in normal pregnancy.

has not been elevated under such circumstances as shown by a number of our cases. This suggests that the mother retains the K for her own requirements and that little or none of the vitamin reaches the infant, or the fetus is unable to utilize it.

The drop in the prothrombin at delivery, shown in Fig. 1, is maintained on the third day post partum and is probably due to a lowered intake of K or to faulty digestion and metabolism during labor. On the other hand, there may be an increased destruction of prothrombin in the lungs. The work of labor was thought to be a factor but this view was discarded on the following evidence:

Five normal subjects, 3 with a prothrombin concentration of 100 per cent, and two with levels of 61 and 68 per cent of normal, respectively, rode a bicycle or played squash for an hour. Immediately thereafter, the prothrombin studies were repeated and no significant decrease was observed in any of the five subjects.

It appears that exercise (i.e., labor) does not lower the prothrombin concentration, indicating that other factors are responsible, i.e., lowered dietary intake and faulty digestion as the patient approaches labor.

During the puerperium, there was no further decrease in the prothrombin due to lactation, since the values were essentially normal at six weeks postpartum.

At the time of delivery, the cord blood of 50 infants showed an average concentration of only 24 per cent of the adult normal. This indicates that the placenta is a barrier to the passage of prothrombin. According to numerous papers in the recent literature, vitamin K administered to the mother produces significant rise in the prothrombin levels of the cord blood. This treatment has been seized upon with regard to prevention of hemorrhagic disease of the newborn. However, if the mothers are deficient (and about 15 per cent seem to be), such treatment would benefit these mothers, which is not a bad idea, but our experience teaches that under such circumstances very little improvement can be expected in the prothrombin concentration of the cord blood. Naumenee, Hellman, and Shettles have recently come to the conclusion that K given during labor does not raise the baby's prothrombin. Originally they were among the first to advocate the use of K in labor.

The marked hypoprothrombinemia of the infant at birth is in itself an indication for the parenteral administration of vitamin K, not to mention the early onset of hemorrhagic disease of the newborn. Javert has reported three cases in which the intrauterine onset of hemorrhagic disease of the newborn was well substantiated. He has also shown further that the disease often occurs on the first day of life. These facts go well hand in hand with the physiologic hypoprothrombinemia (deranged clotting mechanism) of the cord blood and the trauma of labor (capillary rhexis) as etiologic factors in the causation of hemorrhagic disease which calls for parenteral injection of vitamin K to the infant at the time of delivery, as has been suggested by Javert in a discussion of vitamins and pregnancy. It is very probable that parenteral injection of K will become as routine as is the instillation of silver nitrate into the conjunctival sac, and perhaps with greater justification.

There is considerable doubt that the liver of the child is able to metabolize vitamin K during intrauterine life, as suggested by the marked hypoprothrombinemia of the cord blood. It is quite possible that the patent ductus venosus shunts blood around the liver and thereby contributes to liver deficiency as first suggested by Javert and Moore. If this assumption is correct, only when the cord is ligated will the liver begin to function normally with the production of prothrombin so the concentration rises after a few days after an initial drop, as has been observed clinically. To facilitate the formation of prothrombin by the infant, parenteral injection of vitamin K seems indicated immediately after delivery rather than during labor. The practicability of such a procedure was studied in 549 infants as shown in Table I.

In the first series, thyloquinone in corn oil produced local induration at the site of injection in 50 per cent of the infants, and this was invariably absent on the day of discharge from the hospital. When thylohydroquinone was employed, only 11.4 per cent of the infants showed localized reaction, and these cleared up in a few days. Each solution resulted in one abscess which was probably of technical origin. It is of interest that no infant developed hemorrhagic disease of the newborn;

TABLE I. THE PARENTERAL INJECTION OF SYNTHETIC VITAMIN K IN THE NEWBORN

NO. INFANTS TREATED	PREPARATION USED	NO. OF REACTIONS	ABSCESS FORMATION	INFANTS HAVING HEMORRHAGIC DISEASE
196	Thyloquinone, 2 mg. in corn oil	98	1	0
360	Thylohydroquinone, 1 mg. in aqueous solution	29	1	0
Total 556				0

ordinarily, five should have done so, since the clinic incidence of this disease is 0.77 per cent. These studies are being continued at the present time in order to have a larger series of cases. From the evidence at hand, parenteral injection of synthetic vitamin K in the newborn may prevent hemorrhagic disease more effectively than does the maternal administration of the vitamin.

CONCLUSIONS

1. The composite curve of prothrombin concentration was determined in normal pregnancy and the primary trend was upward, with secondary trends having the lowest level in the fourth week, probably due to dietary disturbance caused by morning sickness; while the next low level seen in the twenty-eighth week was probably due to fetal requirements of K.

2. The prothrombin concentration was 70 per cent or below in 15 per cent of 200 normal pregnant women; therefore, they were regarded as having hypovitaminosis K.

3. The cord blood prothrombin concentration at delivery was 24 per cent of normal, while the mothers had a level of 89 per cent of normal. This indicates that prothrombin molecule does not traverse the placental barrier.

4. At term and at the time of delivery, 14 per cent of the mothers were below 70 per cent, and they would have profited by the administration of vitamin K. Studies have indicated that under such circumstances, the mother evidently retains the K for her own needs and that very little if any reaches the fetus, or the child is unable to utilize it.

5. It is probable that the fetal liver cannot utilize K for the production of prothrombin because of the patent ductus venosus. It is only after ligation of the cord that the prothrombin level rises in the newborn infant.

6. Parenteral injections of synthetic vitamin K given to the infant at delivery seem indicated because of the universal hypoprothrombinemia at birth and the early onset of hemorrhage disease of the newborn. Five hundred and fifty-six infants were given synthetic vitamin K at delivery, and hemorrhagic disease did not develop in any of these infants. Under average circumstances, 5 infants should have had the disease. An additional series of cases are being studied for confirmation of this view.

7. The maternal prothrombin level in the puerperium showed no significant deviation due to lactation.

Thyloquinone was provided by E. R. Squibb & Co.

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STUDIES OF THE POST-PARTUM BLADDER

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MEDICAL literature contains very little information concerning the post-partum bladder. This fact is unusual in the light of the tremendous volume of literature on all other parts of the urinary tract in the various periods of pregnancy and the puerperium. Reports and observations dealing with this subject are limited to a few short paragraphs or incidental findings included as a part of a discussion of the urinary tract as a whole.

Most textbooks in obstetrics pass over the subject with generalities about a lack of desire to empty the bladder and with vague descriptions of the trauma to the bladder and urethra incurred during labor.

Stander,[1] in *Williams Obstetrics* where the most complete discussion is found, states that the process of evacuation of the uterus is associated with stretching and trauma of the base of the bladder. Cystoscopic examination after delivery shows not only edema and hyperemia but frequently submucosal hemorrhages.

At times the edema is so marked as to cause obstruction and retention.

The post-partum bladder has an increased capacity and is not so sensitive to intravesical fluid tension. Overdistention is, therefore, common with residual urine. The paralyzing effect of anesthesia and temporarily disturbed function of the nerve supply to the bladder undoubtedly are contributory factors.

In 1906 Holtze[2] found an average of 107 c.c. of bladder residual urine in primiparas post partum and 58 c.c. in multiparas post partum. These all returned to normal within one week.

Stuernagel,[3] in 1912, found that bladder capacity was increased post partum in many cases to a point at which the desire to void did not occur before 1000 c.c. of retention, and it was not unusual for 2,000 c.c. to be tolerated.

In 1921 Walker[4] used a mercury manometer to measure bladder pressure in the male and included in his report the observation "that several puerperal women examined showed evidence of decreased pressure." In 1922 Shutter[5] found that in a small group of nonpregnant women the desire to void occurred at 200 c.c. (this was increased to 350 c.c. at term in the pregnant), but that 800 c.c. produced only slight feeling of pressure post partum. He investigated several patients post partum, using a mercury manometer which showed very low pressure of from 2 to 6 mm. of mercury.

In 1924 Stevens and Arthurs[6] reported a group of 105 pregnant women in which 33 per cent had residual urine. Of 36 patients catheterized on the second day post partum, 29 had residual urine. They believe that trauma and reflex nerve disturbances associated with lowered abdominal pressure result in partial urinary retention immediately post partum.

Textbooks on urology avoid the subject entirely with the exception of Young's *Urology*[7] where Stevens' article is quoted.

With this information at hand a study of the post-partum bladder was undertaken from a standpoint of its cystoscopic appearance and also the intravesical pressure as measured by the cystometer at various levels of bladder capacity.

An effort was made to select a cross section of the patients delivered on the Obstetrical Service of the Los Angeles County General Hospital. All patients delivered from midnight Monday to midnight Tuesday each week were sent to cystoscopic clinic on Thursday morning of that week. The only patients excepted were those delivered by cesarean section. There were 105 patients examined in the first group. Of these

42 were para i
25 were para ii
18 were para iii
7 were para iv
6 were para v
2 were para vi
3 were para vii
1 was para ix
1 was para xii
105

All cases were examined from thirty-six to sixty hours after delivery with an average of forty-eight hours. The age range was fourteen to thirty-six years, with an average age of 23.7 years. The different methods of delivery were divided as follows:

52 were delivered spontaneously without episiotomy
21 were delivered spontaneously with episiotomy
31 were delivered by low forceps with episiotomy
1 breech six-months' fetus after use of bag

Following the examination and observation of the 105 cases, there were 11 operative cases selected as follows for examination:

7 Breech deliveries
2 Midforceps
1 Podalic version and extraction
1 Low cervical cesarean section

Some difficulty was encountered in securing a larger number of midforceps, and in addition most cesarean section cases have indwelling catheter drainage from forty-eight to seventy-two hours routinely.

Baby weights varied from the largest, 10 pounds 5 ounces, to two prematures. The average infant weight was 7 pounds 4 ounces. There was one twin pregnancy.

Duration of labor in stages varies as follows:

First stage, longest 60 hours, shortest 1 hour 25 minutes; with an average of 12 hours 14 minutes.
Second stage, longest 9 hours, 24 minutes, shortest 3 minutes; average 48½ minutes.
Third stage, longest 46 minutes, shortest 2 minutes; average 12.2 minutes.

These patients were allowed to go eight hours before being catheterized. However, the order was discretionary and at times the patients were allowed to go longer than eight hours if there was no discomfort or obvious bladder distention. There were 16 of the 105 cases allowed to go beyond 12 hours before voiding. These varied from fifteen and one-half to twenty-four hours. The amount voided varied between 225 c.c. and 1450 c.c., with an average of 732 c.c. The residual varied from 20 c.c. to 1,100 c.c., with an average of 200 c.c. This obviously was poor post-partum technique. However, no great discomfort compelled the nurses to catheterize before that time. Comparison of these 16 cases with the others shows virtually the same cystoscopic and cystometric findings. Following the first voiding, the volume of residual bladder urine was checked by catheter. There were three of the 105 that were unable to void and required the use of the catheter through the second day. The remainder voided spontaneously in from three to twenty-four hours, with an average of nine and one-fourth hours.

The volume of urine passed at first voiding varied from 100 c.c. to 1,450 c.c., with an average of 478 c.c. Accurate data on residual urine were obtained from 94 of the cases examined, not having been recorded in the remaining 8 cases. Of the 94 patients, 34 per cent had a residual urine in excess of 250 c.c. and in 6 patients, or 6 per cent, in excess of 500 c.c.

METHOD OF EXAMINATION

The patients were brought to cystoscopy without premedication, and 5 c.c. of indigocarmin solution were administered intravenously. A No. 24 Brown-Buerger cystoscope was introduced without anesthesia to the bladder. Appearance time and concentration of indigocarmin from ureteral orifices was observed. The bladder cavity was then carefully inspected for evidence of trauma, inflammation, edema, and distortion, care being taken to avoid overdistention during this procedure.

Following this a No. 18 French Pezzer type catheter was introduced into the bladder cavity. The catheter in turn was connected to an improvised mercury cystometer and the bladder was then slowly filled with sterile water. Readings of vesical pressure in millimeters of mercury were recorded at 250 c.c., 500 c.c., 750 c.c., and 1000 c.c., respectively, except in those cases where some bladder spasm developed or in cases where the distention of the bladder became too painful. While many of these patients experienced no sensations of pain or fullness with the bladder distended to 1000 c.c., it was deemed inadvisable to distend them further.

There was also recorded the bladder volume at the first desire to void and also at whatever point a painful desire developed. An attempt to secure the maximum voluntary pressure was made. However, the variability of cooperation of the patients made this determination difficult to interpret.

CYSTOSCOPIC FINDINGS

Cystoscopic examination of these bladders revealed varying degrees of mucosal congestion and edema, most marked about the bladder neck,

floor, and trigon. This was associated with some distortion of the trigon and floor caused by pressure and protrusion of the enlarged cervix and uterus, the picture being generally that of a congested atonic bladder. Mucosal edema was present in varying degrees but in no cases was it sufficiently marked to be an obstructive factor. In only 19 cases of the entire 116 (of both the original 105 and the selected operatives) were there any evidences of ecchymosis, such as might be expected from direct trauma. In 14 cases the areas of ecchymoses were limited largely to small areas about one or both ureteral orifices. In the remaining 5 cases the ecchymosis involved the greater part of the trigon and base.

Of the 14 patients, 6 were delivered spontaneously with episiotomy and 4 without. Two patients were delivered by low forceps and 2 were breech deliveries. The 2 patients delivered as breeches had very small punctate areas of hemorrhage.

The 5 patients with more or less extensive ecchymosis were delivered, 3 as spontaneous and 2 as low forceps.

The duration of labor in the group showing ecchymosis averaged fifteen hours, fifty-four minutes for the first stage; forty minutes for the second stage; twelve minutes for the third stage. There was only one patient of this group that had a protracted labor, that of fifty-six hours. This comparison does not account for the obvious trauma of the bladder on a basis of length of labor or by difference between spontaneous and operative delivery.

In cystoscopic examination of the 7 breech deliveries, the bladder had the general appearance of that observed in the other cases.

Observation of the bladder in the case of the low cervical cesarean section showed no evidence of ecchymosis. The muscular tone, however, was good. This patient had an indwelling catheter during the first forty-eight hours post-partum.

Indigocarmin dye appeared from the ureteral orifices in an average of five to six minutes after intravenous injection. In 6 cases appearance was delayed from one or the other ureteral orifice more than ten minutes, and in 3 cases no dye appeared from the right ureteral orifice in fifteen minutes.

Other Pathology.—Unilateral duplication of ureteral orifices was noted in two cases and in one case the left ureteral orifice and left ureteral ridges were absent entirely.

CYSTOMETRIC FINDINGS

The normal bladder responds to distention in a characteristic manner. A cystometrogram or a chart recording intravesical pressures, as recorded by a manometer at various degrees of distention, presents a fairly accurate picture of the functional state of the bladder muscle. A normal response is well represented by the following figure which Muschat and others[8] designate as a normal cystometrogram (Fig. 1). Fig. 2 represents a characteristic cystometrogram obtained in the hypertonic group. Fig. 3 represents a characteristic cystometrogram obtained in the atonic or hypotonic group. Fig. 4 represents a composite cystometrogram of this entire series, representing mean average readings of all cases. This shows a definite hypotonic type of curve.

The 105 cases could roughly be divided up into three general groups:

1. Those patients developing painful desire with some bladder spasm before 750 c.c. distention capacity was reached, of whom there were 15.

2. Those patients in whom slight painful desire develops but no bladder spasm occurred to 1,000 c.c. distention, of whom there were 43.

3. Those patients in whom no pain or desire to empty the bladder occurred during distention to 1000 c.c., of whom there were 47.

In the first group, there were fifteen cases, or 14.3 per cent of the total. The average bladder capacity was 610 c.c. and average maximum manometer reading was 33 mm. of Hg.

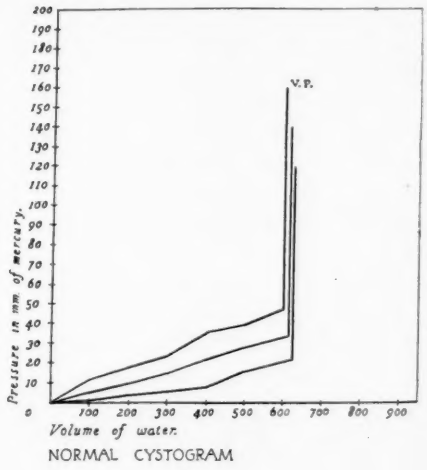

Fig. 1.

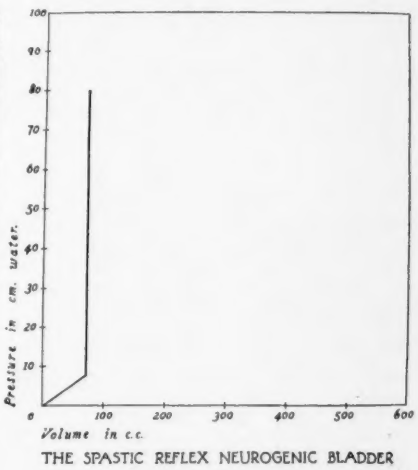

Fig. 2.

Fig. 1.—Cystometric curve, showing maximum, minimum, and average bladder pressures in a group of normal adults, demonstrating gradual increase in pressure up to 600 c.c., then a sharp rise when patient attempts to void.

Fig. 2.—Cystometric curve, showing bladder pressures in spastic neurogenic bladder (compression myelitis). (From McLellan, Frederick C.: *The Neurogenic Bladder,* Charles C Thomas.)

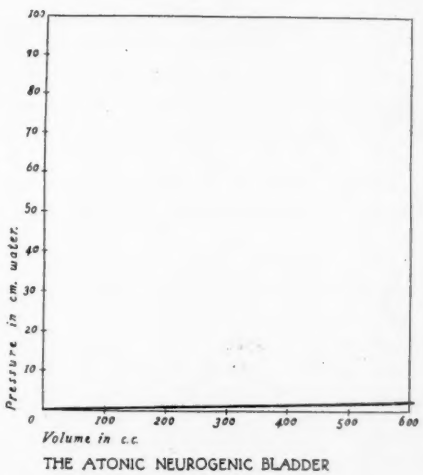

Fig. 3.

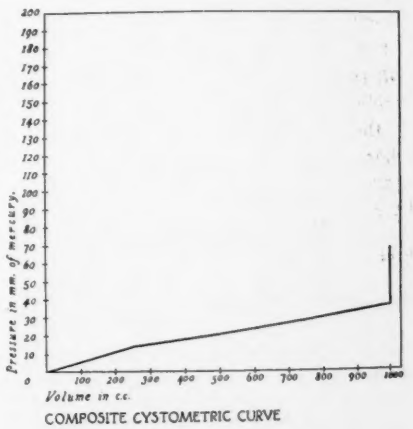

Fig. 4.

Fig. 3.—Cystometric curve, showing bladder pressures in the atonic neurogenic bladder (pernicious anemia). (From McLellan, Frederick C.: *The Neurogenic Bladder,* Charles C Thomas.)

Fig. 4.—Cystometric curve, showing average bladder pressures in the entire group of cases studied. There is a gradual increase in pressure up to 1,000 c.c., then a sharp rise as patient attempts to void. The magnitude of this rise is feeble as compared with the normal.

In the second group there were 43 cases, or 40.9 per cent of the total. The average bladder capacity when this slightly painful desire began was 865 c.c., and the average maximanometer reading was 21 mm. of Hg.

The third group of 47 cases, or 44.8 per cent of the total, had no pain or desire to urinate with the bladder distended to 1000 c.c. The average manometer reading at 1000 c.c. was 14.8 mm. of Hg.

TABLE I. PATIENTS HAVING PAIN OR BLADDER SPASM BEFORE BLADDER DISTENTION HAD REACHED 750 C.C.

	PERCENTAGE OF CASES	AVERAGE MAXIMUM MANOMETER READINGS MM.	AVERAGE BLADDER CAPACITY AT WHICH PAIN OCCURRED C.C.
Group average	14.3	33	610
Patients delivered spontaneously without episiotomy	23.1	31.7	604
Patients delivered with low forceps and episiotomy	9.7	38.7	633
Patients delivered spontaneously with episiotomy	0	–	–

In Table I are shown the types of delivery that make up the group of cases developing bladder spasm together with the comparison of the manometer readings and bladder capacity of each group. There were 23.1 per cent of the patients delivered spontaneously that make up this group and 9.7 per cent of the patients delivered by low forceps. The manometer readings and the bladder capacity show a close correlation of the two types of delivery in comparison with that of the group as a whole.

There were no cases in which the patient was delivered spontaneously with episiotomy that fell into this group. No reason for this can be given. The fact that only 23 per cent of patients delivered spontaneously without episiotomy approached the average cystometric finding would seem significant. In addition, in this whole group the bladder capacity is increased; bladder pressure diminished.

Table II shows the comparison of the group of cases in which painful desire developed with the type of delivery. There is an increase in the number of patients of the group that was delivered spontaneously with episiotomy over either of the other types of delivery. The average bladder capacity and the manometer reading show a very close correlation. No reason for the increase in the spontaneous group with episiotomy can be given.

TABLE II. PATIENTS HAVING PAINFUL DESIRE TO VOID WITH BLADDER DISTENDED TO 750-1000 C.C.

	PERCENTAGE HAVING PAINFUL DESIRE TO VOID	AVERAGE MAXIMUM MANOMETER READING MM.	BLADDER VOLUME AT WHICH PAINFUL DESIRE OCCURRED C.C.
Group average	40.9	26.7	866
Patients delivered spontaneously without episiotomy	28.8	23	872
Patients delivered spontaneously with episiotomy	66.6	29	873
Patients delivered with low forceps and episiotomy	41.9	20.6	852

In Table III is shown a comparison of the group of patients without pain or desire to void at 1,000 c.c. of bladder distention and the type of delivery. The close relationship between the percentage of the cases of each type of delivery with that of the percentage of the group as a whole is noteworthy. The manometer readings at 1,000 c.c. fall well within the range of that found in the atonic bladder.

Table IV shows the comparison of the general average with that of the 7 breech deliveries.

NO PAIN	SLIGHT PAIN	
57 per cent at 1,000 c.c.	29 per cent at 962 c.c.	14 per cent spasm at 650 c.c.

The two patients with midforceps delivery both had pain at 900 and 950 c.c.; however, both were taken to 1,000 c.c. where the manometer readings were 16 and 11 mm. of mercury, respectively.

There were 20 patients of the 105 that received a light ether anesthetic at the time of delivery but no ante-partum analgesia. The remainder received nembutal and scopolamine in varying amounts from 3 to 7½ ss. gr. of nembutal and one to two doses of 1/150 gr. of scopolamine.

Table V shows a comparison of these two groups and the percentage of the bladder type in each. They both come within close range of the general average for the whole group.

TABLE III. PATIENTS HAVING NO PAIN WITH BLADDER DISTENDED TO 1000 C.C.

	PERCENTAGE HAVING NO PAIN	MAXIMUM AVERAGE MANOMETER READING MM.
Group average	44.8	14.8
Patients delivered spontaneously without episiotomy	48.1	15.6
Patients delivered spontaneously with episiotomy	38.0	13.6
Patients delivered with low forceps and episiotomy	45.1	13.4

TABLE IV. PATIENTS HAVING NO ANALGESIA BUT LIGHT ETHER ANESTHESIA

	NUMBER OF CASES	PERCENTAGE OF CASES HAVING NO PAINFUL DESIRE UP TO 1000 C.C.	PERCENTAGE OF CASES HAVING PAINFUL DESIRE 750-1000 C.C.	PERCENTAGE OF CASES HAVING PAIN OR SPASM BELOW 750 C.C.
Patients having light anesthesia but no analgesia	20	55	40	5
Group	105	44.8	41	14.2

TABLE V. COMPARISON OF SELECTED GROUP OF ELEVEN BREECH AND OPERATIVE DELIVERIES WITH THE GROUP OF 105 ROUTINE DELIVERIES

	TOTAL NUMBER OF CASES	PERCENTAGE HAVING NO PAIN AT 1000 C.C.	PERCENTAGE HAVING PAIN AT 750-1000 C.C.	PERCENTAGE HAVING PAIN AT 750 C.C. OR LESS
Group of routine deliveries	105	44.8	41.0	14.2
Group of breech and operative deliveries	11	45.5	36.3	18.2

COMMENTS

As seen through the cystoscope, the bladder post partum presents a pale slightly edematous mucosal surface. The bladder wall itself is relaxed and atonic. When deflated it collapses in folds like a paper sack rather than contracting as a normal elastic structure.

Kidney function as evidenced by the use of indigocarmin intravenously in the vast majority of cases falls well within normal limits.

Except for a few cases, mucosal injection, submucosal hemorrhages, and marked edema, such as would be expected from gross trauma, are conspicuous by their absence.

It would be reasonable to assume that bladder trauma would be increased in prolonged labor, in difficult forceps deliveries or in breech deliveries with pressure from above on the aftercoming head. However, a comparison of the 7 breech deliveries with the group of 105 cases originally examined showed no higher incidence of direct bladder trauma. This was also borne out in the two cases of midforceps, the cesarean section and the version and extraction. In the main these patients all come in the same general category, exhibiting little direct bladder trauma. The few cases of this series showing moderately extensive ecchymosis varied very little in their functional response from those showing none. Trauma does not seem to account for the dysfunction of the bladder.

Cystometrograms portray graphically with fair accuracy the functional state of the bladder muscle. Bladder disturbances as pictured by the cystometrogram may be divided roughly into two main groups, the hypertonic or spastic type with increased muscle tone and increased capacity. Each of these groups may be on the basis of myogenic or neurogenic disturbances.

As a group, the post-partum bladder falls into the hypotonic group with decreased bladder sensation, reduced muscle tone and increased capacity. Further comparison of the 105 routine cases with the selected operative case cystometrically shows a surprising similarity of response to distention of the bladder with water. The patient delivered by version and extraction and the two patients delivered by mid-forceps show the same lack of bladder tone. The low cervical cesarean section after two days of bladder rest with an indwelling catheter showed spasm at 650 c.c. capacity and a much better bladder tone.

The anatomical site and nature of this disturbance is not explained. Whether it is primarily neurogenic or myogenic in origin is not known. The fact, however, that past studies have shown this disturbance to be only temporary in nature would indicate that no permanent changes have occurred in either muscle or nerve tissue.

It would seem reasonable in the light of the above findings that post-partum management of the bladder should be directed at alleviating prolonged overdistention and avoiding the ever present threat of urinary stasis. We perhaps should become more bladder conscious of our post-partum cases. It is not inconceivable that prolonged overdistention

post-partum may be a factor in the formation of cystocele in the presence of injury to the bladder base. Further studies will be necessary to determine the exact nature of the dysfunction encountered in these cases.

SUMMARY

1. Cystoscopic examination of 116 post-partum bladders revealed general relaxation and minor degrees of mucosal edema.

2. Ecchymosis of bladder mucosa was present to a minor degree in 12 per cent of the cases and to a moderate degree in 4.3 per cent of the cases. This was not increased by breech extraction, nor was it seen in two cases of midforceps, one case of version and extraction and one low cervical cesarean section.

3. Cystometric studies revealed hypotonic bladders with decreased bladder sensation and increased capacity in 86.2 per cent of the entire series.

4. Type of delivery, trauma, and prepartum analgesia do not account for this dysfunction.

5. A plea is made for attention to the relief of overdistention of the post-partum bladder.

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From an analysis of a large series of cases, the author found perisigmoidal adhesions in 20 per cent of all women subjected to laparotomy. These adhesions were most common during the reproductive years and reached their maximum at the age of thirty. These adhesions arise most probably from septic or aseptic inflammatory conditions of the internal genitalia; second, from the sigmoid itself; and third, from the appendix or small bowel. Perisigmoidal adhesions produce no marked symptoms, and there is no definite symptom complex by which the diagnosis can be made. The majority of patients complained of chronic obstipation and irregular pains in the left lower quadrant of the abdomen and these are not characteristic symptoms. In the majority of the cases therefore, no preoperative diagnosis of such adhesions was made. Perisigmoidal adhesions are found most frequently in connection with disease of the left adnexa, with retroversion of the uterus, and with fibroids or adnexal tumors. In many instances, the adhesions are of no clinical significance and when found may be left undisturbed. When they are massive and produce distortion and/or traction, they must be resected. The author insists that during the course of every laparotomy, the pelvis must be carefully examined for such perisigmoidal adhesions. Obviously, resection of such adhesions must be followed by careful and complete peritonization in order to prevent recurrence. Attempt must be made in every instance to restore the sigmoid to its normal position and mobility.

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PLACENTAL BLOOD PLASMA

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THE therapeutic value of adult blood plasma is well established. However, the difficulty in securing blood in sufficient quantities in many hospitals in order that pooled plasma can be safely prepared, particularly where there is no blood bank, stimulated us to investigate placental blood as a source of plasma, and to determine the value of such plasma in clinical use.

Polayes, Lederer and Wiener[1] found in a series of 500 infants, where the Landsteiner blood groups were studied that 283, or 56 per cent, of these infants had no demonstrable specific blood group agglutinins in their serum at birth. Thomsen (cited by Wiener[2]) has shown that in those infants where the blood agglutinins were found to be present they had a very low titer. Because of this lack of specific blood group agglutinins or their very low titer plasma prepared from placenta blood can be considered safer than adult plasma even though small amounts be pooled. This then should be an ideal source of plasma, especially for a small hospital which cannot avail itself of large amounts of adult blood for the preparation of plasma.

We found that sterile plasma can be obtained from placental blood in worth-while quantities. An average of 103 c.c. of whole blood was derived from each placenta, in a series of 200 placentas from which the blood was collected. From 128 c.c. of citrated placental blood, we have obtained an average of 70 c.c. of consistently uncontaminated citrated plasma (25 c.c. of 2.5 per cent sodium citrate solution being placed in each collecting bottle).

Before using placental plasma clinically, we reviewed the literature for comparative analysis of adult and fetal plasma and found that chem-

TABLE I. ANALYSIS OF THE VARIOUS PROTEIN COMPONENTS OF ADULT AND PLACENTAL PLASMA AS DETERMINED BY ELECTROPHORESIS

	FRESH ADULT PLASMA TYPE A (3)* pH 7.72	PLACENTAL PLASMA (21)* pH 7.85
Albumin per cent	3.96	3.47
Albumin/globulin†	2.27	2.00
Alpha globulin albumin	0.08	0.13
Beta globulin albumin	0.18	0.16
Gamma globulin albumin	0.18	0.21
Fibrinogen albumin	0.08	0.05
	Citrated	Oxalated

*Refers to number in Fig. 1.
†Calculated on serum basis.

ically there is very little difference between the two. Furthermore Scudder[3] has recently pointed out that there is very little difference even in the electrophoretic pattern of the proteins found in adult and placental plasma, and he states that placental blood may be considered a normal

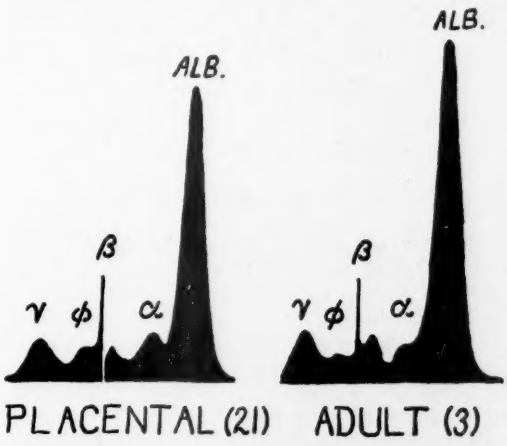

Fig. 1.—The electrophoretic protein patterns of the placental and adult plasma.

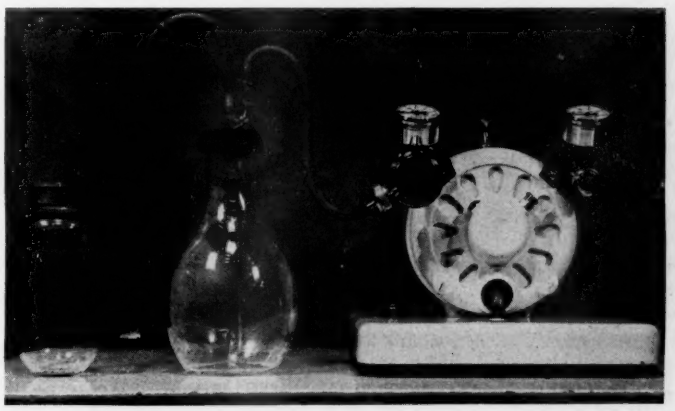

Fig. 2.—The 225 c.c. collecting bottle is shown with the spoon tipped suction tube, bottle into which the plasma is pooled and the electric suction pump. This closed system for pooling the plasma minimizes the possibility of contamination.

source of conserved blood.* The various protein constituents which make up adult and placental plasma together with their electrophoretic curves are reproduced for comparison with Scudder's permission in Fig. 1 and Table I.

*Through the courtesy of Longsworth of The Rockefeller Institute, we have confirmed the findings of Scudder. Electrophoretic patterns have been made on plasma prepared from the blood of the mother and from placental blood obtained at the time of her delivery, and they show a marked similarity.

As a routine "Seconal"* is used for analgesia on the obstetric service in this hospital. We felt that the concentration of this drug in placental plasma might contraindicate its used. Therefore a barbituric acid determination was made on Lot 23 which represented 250 c.c. of plasma, pooled from the placentas of 4 patients who had received a total of 1 Gm. of this drug. A concentration of 5.2 mg. per 100 c.c. was found to be present in this 250 c.c. In our experience no hypnotic or sedative effect is produced until the concentration in the blood has reached 20 to 30 mg. per 100 c.c. This laboratory finding confirmed our clinical observation that such a small amount of this barbiturate does not contraindicate the use of pooled placental plasma.

TECHNIQUE

Collection.—The blood is taken from the cord immediately after the birth of the child, prior to the expulsion of the placenta and before any perineal repair is made. The cord is clamped and cut two inches from the umbilicus. A "sterile" assistant immediately cleans it with tincture of "zephiran"† solution 6 to 8 inches proximal to the clamp. The cord is then grasped, compressed with a sterile towel, and severed a short distance from the clamp with another pair of sterile scissors. The "clean" cut end is again cleaned with tincture of "zephiran" solution and inserted into a 225 c.c. graduated, round bottom centrifuge bottle (Fig. 2) into which has been placed, prior to sterilization 25 c.c. of 2.5 per cent sodium citrate solution. The flask and cord are wrapped in the sterile towel and held by the assistant, thus preventing any contamination by amniotic fluid. The cord is then milked to express the blood while pressure is made on the uterus to fill the cord with the blood which remains in the placenta. The flask is covered with a sterile rubber cap to hermetically seal it for transportation. The yield of blood has been greater and the possibility of contamination less when the blood has been obtained prior to the separation of the placenta. This technique is not complicated, and the blood can be collected in a few minutes. A serologic test for syphilis is made on blood obtained from the placenta and the mother after delivery.

Preparation.—The blood is placed in a refrigerator at 4 to 6° C. We have obtained a yield which warrants collection by allowing the blood to settle for five or six days and then separating the plasma. However, routinely we centrifuge the blood within twelve to twenty-four hours, and separate the plasma. By this latter technique we have been able to increase the yield of plasma 10 per cent.

By means of an electric suction pump and a 1 c.c. pipette or the special spoon tip suction tube shown in Fig. 2, the clear plasma is removed and pooled in lots of 250 c.c. By decreasing the suction so that a drop at a time can be delivered into the flask, we have found that almost all the plasma can be obtained. When an electric suction pump is not available, a water or hand suction pump can be used satisfactorily. From each 250 c.c. of pooled plasma, 10 c.c., in this series, were taken for culture. To the remainder of the pooled plasma 250 c.c. of 5 per cent glucose in normal salt solution were added, following the advice of Elliott, Busby and Tatum.[5] We have noticed that there is less precipitation in placenta plasma than in adult plasma observed at similar intervals of time after preparation, this being partly due to the lower total fat content of placental plasma. To each 500 c.c. of this diluted plasma, 5 c.c. of a 1 per cent solution of aqueous "merthiolate"‡ are added as a preservative.

Employing the rigid technique outlined, we have not obtained a single positive culture, despite the fact that every 250 c.c. of pooled

*Seconal-Sodium propyl-methyl-carbinal allyl barbiturate—Lilly.

†Zephiran: Tincture of a mixture of high molecular alkyl-dimethyl-benzyl-ammonium chlorides. Used because of a high germicidal potency and its rapidity of action.[4]

‡Sodium ethyl mercuri thiosalicylate—Lilly.

plasma has been cultured aerobically and anaerobically before diluting. Aerobically it is cultured on blood agar plates in plain dextrose brain broth* as well as in dextrose brain broth to which has been added 5 c.c. of whole adult blood. Anaerobically it is cultured on blood agar plates in a carbon dioxide jar.

We have varied the technique of collecting placental blood in several ways. Bacteriologic study shows that blood obtained from the cord without a "cleanup" has given a positive culture, but after employing the technique which we have developed, blood obtained from the same cord has given a negative culture. On the basis of this work we believe the high percentage of positive cultures obtained by Fine, Alter, and Baptisti[6] and Boland, Craig, and Jacobs[7] was due mainly to faulty technique during collection of placental blood. Blood has not been taken from patients in whom the membranes have been ruptured for forty-eight hours or longer nor from those in whom there is any evidence of disease which might be transmitted to the fetus by the mother.

CLINICAL USES OF PLACENTAL PLASMA

To date we have used placental plasma in 30 varied clinical conditions. The results have been very gratifying in the clinical response shown and in the complete absence of any local or systemic reactions following its administration.

In four of the patients we used plasma to combat hypoprotonemia. This in two was associated with cardiac failure, in one with carcinoma of the rectum with associated malnutrition, and another in a child, aged 4½ years, with acute glomerulonephritis. In all of the patients there was definite clinical improvement as well as laboratory evidence of an improved plasma protein. The improvement noted in the case of acute glomerulonephritis was most gratifying. For, following the administration of placental plasma, a fall in blood pressure and disappearance of the edema occurred. Prior medical treatment had failed to produce any change.

In four of the cases the placental plasma was given to patients with infections and associated dehydration. The first two were premature infants to whom the diluted plasma was given subcutaneously in doses of 30 to 60 c.c. for two or three days. The clinical response in these two cases was dramatic. The third, a fifteen-day-old infant with an infectious diarrhea received the plasma in the same manner. In these three cases we were able to give subcutaneously a fluid whose electrolyte balance and whose plasma protein were exactly that of the normal infant. The fourth, an adult patient, acutely ill with otitis media and mastoiditis received 800 c.c. of the diluted placenta plasma intravenously and showed definite clinical improvement.

Seventeen of the patients to whom the plasma was given were in shock at the time of administration. The etiology of the shock was due to a variety of causes, such as: incomplete abortion with hemorrhage, operative shock occurring during cesarean section, operative shock during a radical mastectomy, shock associated with first and second degree burns, hemorrhage from a gastric ulcer, hemorrhage from varices of the colon and premature separation of the placenta with concealed hemorrhage. This latter patient who had been treated by the usual routine of morphia and intravenous glucose solution showed signs of improvement which lasted for only a short while. The patient again showed signs of shock just prior to and during a cesarean section. As there was not time to procure a donor for a whole blood transfusion, 500 c.c. of pooled placental plasma were given. This effectively combated the shock, despite the fact that laboratory evidence revealed the patient had sustained a

*Dextrose brain broth.

1 calf brain	
Delfco nutrient broth	8 Gm.
Sodium chloride	8 Gm.
Dextrose	2 Gm.
Andrade's indicator	7 c.c.
Distilled water	1,000 c.c.

marked blood loss. By adding plasma whose coagulating properties have been stated by Goodall, Anderson, Altimas and MacPhail[8] to be 25 to 30 times that of adult blood, we believed that this reduced the amount of blood which the patient lost during the remainder of the operation and postoperatively. This patient made an uneventful recovery and no transfusion of whole blood was necessary. One patient in shock following subtemporal decompression and removal of an epidural hematoma associated with fracture of the skull responded very well to dehydrated placental plasma. This was dissolved in distilled water to four times its normal concentration.

A summary of the case of one patient in shock following an abortion with hemorrhage is given. The dramatic response of this patient to the placental plasma is shown in Fig. 3. In this case as in many of the others where the shock was acute and the shock combating agent urgently needed, the placental plasma bank offered the necessary therapeutic agent.

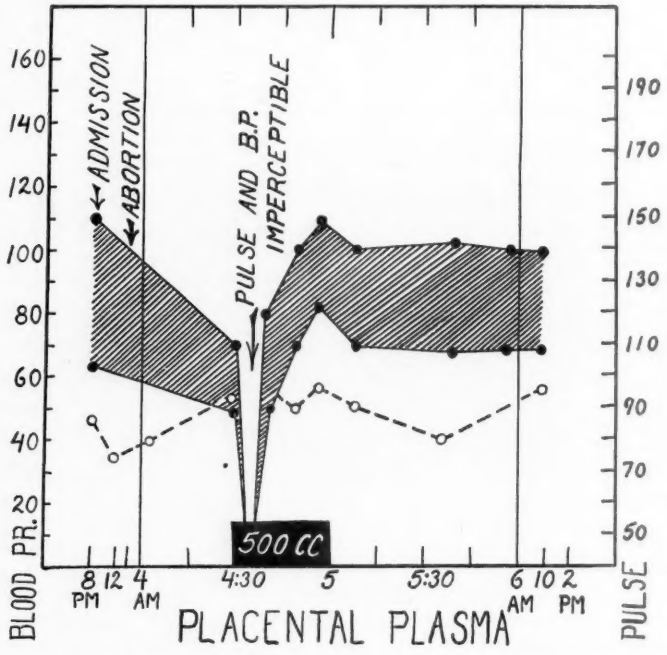

Fig. 3.—(Case 1.) Shock following abortion with hemorrhage, showing effect of placental plasma on pulse rate and blood pressure.

CASE REPORT

CASE 1.—E. B., a white female, aged 32 years, multipara, quintigravida, was admitted to the Union Memorial Hospital at 8:15 P.M. on Oct. 23, 1940, with a history of cramp-like lower abdominal pains of four hours' duration. On admission the patient was pale, weak, and complained of abdominal pain and vaginal bleeding. The blood pressure was 110 systolic and 65 diastolic, pulse 86 beats per minute, and the hemoglobin was 11 Gm. The bleeding increased in amount and the abdominal pain became more severe during the next two hours, despite the administration of morphia. Six hours after admission the patient aborted a five months' fetus, but bled profusely before the placenta and membranes could be expressed. Two hours after the abortion the blood pressure dropped to 70 systolic and 48 diastolic, and the pulse at this time was very irregular and hard to count. Ten minutes later the pulse and the blood pressure were imperceptible. At this time 500 c.c. of diluted placental plasma were given intravenously. When 250 c.c. of the plasma had been given, the blood pressure rose to 80 systolic and 50 diastolic while the pulse rate was

92 beats per minute. Fig. 3 shows the steady rise in blood pressure which followed. The blood pressure just after the plasma had been given was 110 systolic and 80 diastolic with a pulse rate of 100 beats per minute. Six hours later the blood pressure was 100 systolic and 60 diastolic. Convalescence was uneventful and a transfusion of whole blood was not necessary.

In all of the patients, satisfactory results were obtained with adequate dosage and in not a case was there any systemic or local reaction following the administration of the placental plasma. This was true despite the fact that the placental plasma used in some of the cases was less than twenty-four hours old. In some it had been diluted with 5 per cent glucose in normal salt solution and stored from two to thirty days, while in others it has been frozen and subsequently liquefied for intravenous administration. In others it had been desiccated and given in a concentration four times normal.

Encouraged by our results, we have built an inexpensive but extremely satisfactory dehydration apparatus, to be described in a later publication. The dried placental plasma used in the above cases was prepared by this method. At present we are dehydrating pooled placental plasma obtained from the obstetric service of another hospital as well as from our own, and have demonstrated to ourselves that this is very practical; and for this reason we feel that in a time of a National emergency placental blood from several hospitals in a large city could be transported to central depots for the preparation and storage of plasma in quantities. We are now dehydrating placental plasma for storage and for further clinical investigation, particularly with reference to the effect of dried placental plasma on wound healing, following the suggestion made personally to us by Gey and Gey who have reported[9] the use of placental serum over a period of twelve years for the growth of cells in continuous culture and have demonstrated a "growth sustaining" substance in placental serum. This is in contradistinction to the "growth inhibiting" substance found to be present in adult serum by Carrel and Ebeling.[10] If our preliminary experiments are substantiated, the use of dried placental plasma locally to stimulate cell growth may offer a definite advance in the treatment of wounds.

SUMMARY

A heretofore disregarded source of human plasma* is discussed together with a method for its collection, preparation, and preservation; the advantages as well as the safety and the therapeutic value of plasma from this source are outlined.

CONCLUSIONS

1. Placental blood can be used as a source of human plasma.

2. Placental plasma can be prepared, stored, transported, and used in all ways in which adult plasma can be similarly handled.

*Since this article was submitted for publication, the author's attention has been attracted to a reference to the use of placental blood as a source of plasma by Mahoney, Kingsley, and Howland: Ann. Surg. 113: June, 1941.

3. Chemically and physiologically there are no objections to the use of placental plasma.

4. Placental plasma can be administered after the usual methods of preservation to patients on a diversity of indications with absolute safety, without local or systemic reaction.

5. Clinically, placental plasma is equal in therapeutic value to adult plasma, and its general use may prove to be more satisfactory.

6. With very little effort any hospital with or without a blood bank but with a maternity service can prepare blood plasma for clinical use.

7. In the time of a National emergency, military or otherwise, placental blood heretofore discarded can be collected and sent to depots for the preparation of plasma and the storage of this valuable therapeutic agent.

Dr. John G. Murray, Jr., was responsible for the initiation of this investigation.

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MANUAL REMOVAL OF THE PLACENTA

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THE frequency with which manual removal of the placenta is performed differs considerably in the reports of various clinics. The range of variation is given as between 0.051 per cent and 3.25 per cent (Table I).

A study of the available statistics seems to indicate that no marked change in the frequency of manual removal has occurred in recent years. Between 1883 and 1918 figures range from 0.34 per cent to 1.8 per cent; from 1928 on, between 0.3 per cent and 3.27 per cent.

Notwithstanding the apparent absence of change in incidence, the number of maternal deaths due to manual removal has sharply decreased in recent years. A review of the literature (Table I) indicates a mortality range in the older reports of between 10 per cent and 15.4 per cent. In contrast to this, the more recent reports indicate that the mortality rate varies from 1.5 per cent to 5.0 per cent, with an absence of fatal results in some of the more recent series.

This decrease in maternal mortality is understandable when considered in the light of more recent additions to the obstetrician's armamentarium, notably, intravenous glucose, blood transfusions, more widespread use of intravenous oxytocics, and the tendency to perform manual removal before and not after the symptoms of shock have supervened. The appropriate treatment of shock due to loss of blood is today more and more recognized as being most necessary before manual removal is attempted.

TABLE I. LITERATURE ON MANUAL REMOVAL OF THE PLACENTA

AUTHOR	YEAR	TOTAL NO. OF DELIVERIES	NO. OF MANUAL REMOVALS	INCIDENCE %	MORTALITY %	MORBIDITY %
Ssolowjew	1883-1918	304,192	2,912	0.95		
	1918-1933	179,717	2,527	1.40		
Adlerakraus	1894-1907	40,000	452	1.13	0	
Leo	1910	22,250	329	1.48	7.9	
Alletsee	1912	7,125	131	1.80	7.7	
Brandt	1917		30	1.8	0	34.4
Baum	1900-1920	20,418	248	1.20	2.8	34.7
Borberg	1910-1918		50		10.0	60.0
Goethals	1924	16,486	60	0.36	6.6	
Laubenberg	1929	30,000	780	2.60	1.85	
Johannsen	1931	500	26	5.2	0	
Currie	1932				15.4	
Fahlbusch	1932	81,175	1,050		3.15	
Sejrsai	1934			0.51	1.7	80.6
Granzow	1934			1.94	1.6	
Karlin	1935			1.15	0.0	12.1
Peckham	1935				10.7	
Kristensen	1935	16,137	208	1.30	2.0	49.2
Letinsky	1935			2.20	2.0	20.0
Block	1937	50,545	386	0.76	3.6	
Schie		17,133	189	1.10	1.58	
Littaver		10,978	59	0.54	3.4	

Older Mortality Statistics Cited by Eastman

AUTHOR	MORTALITY %
Rosenthal, 1899-1900	13
Vogel, 1903	13.5
Hegar, 1862	11.0

We were able to accumulate from a total of 7,132 deliveries 62 cases of retained and adherent placentas in which 56 manual removals were performed, an incidence of 0.78 per cent. Twenty-four of these were service cases, the rest were patients on the private pavilion. Out of 56 cases of manual removal performed, there was one maternal death, a mortality rate of 1.78 per cent.

CASE 1.—B. S., aged 33 years, a tertigravida. The first pregnancy terminated in the delivery of a stillborn fetus, and the second (two years later) in a live child delivered by cesarean section, performed because of a transverse presentation. On Sept. 11, 1939, at 5:25 A.M. she was admitted to the private maternity in active labor with ruptured membranes, and a diagnosis of a footling presentation was made. At 3:05 P.M. delivery from below was attempted although dilatation of the cervix was not complete. The feet and trunk were extracted, but the delivery of the head was impossible until Dührssen's incisions were made. A still-

born fetus weighing 6 pounds 4 ounces was delivered and the cervical lacerations which extended somewhat were repaired. The placenta failed to separate, and after one hour and twenty-five minutes, because of profuse hemorrhage, manual removal was done with great difficulty and in piecemeal fashion. Following this, the bleeding was controlled but the condition of the patient was only fair.

At 5:45 P.M., about one hour and a quarter later, the patient went into profound shock and suddenly died. Permission for autopsy could not be obtained and no pelvic examination was made, so the possibility of uterine rupture cannot be ruled out.

Comment.—Several errors in the handling of this case are obvious. The attempt to deliver the patient with a partially dilated cervix, and the delay in the manual removal in the face of active bleeding both contributed to bring about this fatality.

An excellent example of improper treatment with a failure to utilize blood transfusions and early removal of an adherent placenta is demonstrated by the following case history.

CASE 2.—R. B., aged 26 years, primigravida; estimated date of confinement was Sept. 10, 1938. The prenatal course was entirely uneventful until September 15, when at 6:00 A.M. she was found unconscious on the floor at home, in a pool of blood (estimated blood loss at this time was 500 c.c.). On admission to the private maternity division, she was bleeding moderately, the pulse was rapid and feeble, but the blood pressure was 120/80. The fetal heart could not be heard. Examination revealed a fully dilated cervix, with the membranes bulging, and the head high. The membranes were ruptured, the head descended into the pelvis, and bleeding ceased. Blood loss in this period, since admission to the Hospital was between 800 and 1,000 c.c. At 8:25 A.M. spontaneous delivery of a stillborn fetus weighing 6 pounds 10 ounces occured, and immediately following delivery of the child hemorrhage again became profuse. The placenta could not be expressed by rather vigorous Credé method.

At this time the pulse was imperceptible, the patient cyanotic, and in a marked state of shock. Intravenous glucose, caffeine, Trendelenburg position, and external heat were all utilized. Bleeding persisted and respirations ceased at 9:40 A.M. The placenta removed after death was very adherent, partially separated, and came away from the uterine wall piecemeal.

MORBIDITY

Infection complicated the puerperium in 26 (41.93 per cent) of the 62 cases of retained and adherent placentas. Puerperal morbidity is high in most of the series reported, varying from 15 to 80 per cent. It is noteworthy that in the six instances in which spontaneous separation of the placenta finally occurred, only once did elevation of temperature occur in the puerperium; that patient developed a severe thrombophlebitis in the left leg and remained in the hospital for sixty days.

Letinsky (1935) and Block (1937) found that the frequency of morbidity was greater among cases of retained or adherent placentas necessitating manual removal after an operative delivery than in those

TABLE II. MORBIDITY

NORMAL DELIVERIES	LETINSKY	BLOCK	MOLDAVSKY AND SOLOWAY
Noninfected	12%	23.2%	32.30%
Operative deliveries	18%	54.4%	46.15%

in whom the placenta was delivered manually following spontaneous delivery. A similar conclusion can be drawn from our own series.

Fetal Mortality.—Four fetal deaths (6.45 per cent) occurred. Two were deaths in utero, one because of nephritic toxemia and the other due to premature partial separation of the placenta. The other two were premature babies which died during the neonatal period.

Parity.—The fact that the patients in this series were almost exactly evenly divided into primiparas and multiparas seems to rule out parity from the list of possible etiologic factors responsible for adherent and retained placenta. Of significance, however, is the fact that of the women who were pregnant for the first time, 17 or more than half, were elderly primiparas. This adds but another unfavorable possibility to the hazards of pregnancy in this age group.

Obstetric History.—An abnormal obstetric background was found in 22 cases (35.48 per cent). Table III shows that in thirteen instances, or 59.09 per cent of the cases with previous pathology, there was a history of one or more septic abortions.

TABLE III. OBSTETRIC BACKGROUND

NAME	AGE	GRAVIDITY	OBSTETRIC BACKGROUND
L. B.	33	iii	One miscarriage
T. W.	27	ii	Breech
J. B.	23	iv	One ectopic pregnancy, two miscarriages
K. B.	23	ii	Six abortions (one infected)
S. T.	23	iv	Three infected abortions
M. S.	30	iv	One miscarriage
R. E.	28	ii	One premature labor
M. P.	34	ii	Pyelitis of pregnancy
L. K.	27	ii	One miscarriage
J. R.	21	ii	Neonatal death
M. G.	30	iv	One miscarriage
A. K.	25	ii	Breech, premature labor
J. D.	21	iv	Dilatation and curettage after third pregnancy
A. A.	31	ii	Section for fractured pelvis
B. S.	31	ii	Two miscarriages
S. T.	29	ii	Induced abortion
D. S.	30	ii	Manual removal with first pregnancy
D. B.	31	ii	Incomplete abortion
F. E.	30	iii	High forceps with first pregnancy Dilatation and curettage after miscarriage
E. K.	21	ii	Premature labor
M. S.	24	ii	One miscarriage
R. R.	28	ii	One miscarriage

The frequency of previous uterine infection, with probable injury to the uterine endometrium lends credence to the concept of intrauterine abnormality as a predisposing agent in the production of an adherent placenta.

Prenatal Period.—The prenatal course of 30 per cent of the patients comprising this series exhibited abnormal trends. From Table IV it is evident that toxemia of pregnancy was by far the most frequent complication.

TABLE IV. COMPLICATIONS OF PRENATAL PERIOD

COMPLICATION	NO. OF CASES	PER CENT
Toxemia	9	47.36
Breech presentation	4	21.05
Late ante-partum hemorrhage	3	15.78
Threatened abortion	2	10.52
Pyelitis	1	5.26

The unusual incidence of late post-partum hemorrhage is worthy of note. The significance of the increased frequency of breech presentations is not clear.

Labor.—The average duration of labor was twenty-three hours and twenty-three minutes, and varied from two hours to three days. As was expected, labor was characterized by a definite tendency to uterine inertia. In nine instances this was the only apparent basis for prolonged labor. As a matter of fact in this group, the average length of labor was fifty hours. The average duration of the third stage of labor was one and one-half hours, and ranged in length from fifteen minutes to four hours and fifteen minutes.

In 46 instances, the placenta was described as being adherent, fibrotic, and difficult to separate from the uterine wall. The placenta was retained in 10 cases, and in all of these was described as being free in the lower uterine segment. In 6 of the records there was no description of the presence or absence of true adherence of the placenta to the uterine wall.

TABLE V. INDICATIONS FOR MANUAL REMOVAL

INDICATIONS	NO. OF CASES	PER CENT
Hemorrhage	20	32.25
Unsuccessful Credé	22	35.49
Other causes:		
Toxemia, prompt delivery Hourglass cont. of uterus Delayed separation (More than 1 hr.)	9	14.15

Severe hemorrhage complicated the deliveries in 20 cases, or 42 per cent, blood loss varying from 500 to 1,800 c.c. Only one of these was in the retained placenta group, the rest all occurred in those instances in which the placenta was adherent and fibrotic in character. Transfusions were given in 11 of these cases, almost 50 per cent.

Remote Sequelae.—Schie, by means of mailed questionnaires to all the patients in his series on whom manual removal of the placenta had been performed, found that out of 145 patients, 32, or 21.9 per cent, were living in involuntary sterile marriage.

Through the cooperation of our Social Service Department we were able to obtain accurate follow-up studies on 13 of the 24 ward cases.

Seven had become pregnant since the manual removal performed in every instance following a first pregnancy. In greater detail their stories are as follows:

CASE 1.—H. P., 25 years of age. First pregnancy in 1938 with manual removal of the placenta; second pregnancy in 1940. The second pregnancy was complicated

by premature separation of the placenta three weeks prior to term, with an estimated blood loss of 1,000 c.c. Spontaneous birth of a live baby occurred.

CASE 2.—M. R., 35 years of age. First pregnancy in 1928 with manual removal; four pregnancies since (1929, 1930, 1931, 1935). No difficulties, all spontaneous deliveries, the placenta separated spontaneously and quickly after each delivery.

CASE 3.—M. T., 23 years of age. First pregnancy in 1938; second pregnancy in 1940. Forceps delivery, spontaneous separation of placenta within ten minutes after delivery of the baby.

CASE 4.—B. P., 23 years of age. First pregnancy in 1937. At present six months pregnant, uneventful to date.

CASE 5.—G. F. First pregnancy in 1935; second pregnancy in 1936. Second pregnancy terminated in spontaneous abortion. Has desired to become pregnant since, and cannot.

CASE 6.—D. S., aged 31 years. First pregnancy in 1938. Delayed separation of the placenta, with her second pregnancy in 1940. Spontaneous separation occurred after a thirty-seven-minute waiting period.

CASE 7.—D. H., aged 24 years. First pregnancy in 1940. The patient was readmitted to the dispensary April 28, 1941, about five months pregnant. Because of the complications that marred her first pregnancy, namely, toxemia, manual removal, and thrombophlebitis, she was followed at two-week intervals. On May 13, 1941, the sixth month of her pregnancy, she was admitted to the ward, with a history of vaginal bleeding and with irregular pains. She went into active labor and after thirteen hours and thirty minutes, delivered spontaneously a premature stillborn child, breech presentation. The fetus showed softening of the skull bones and maceration of the skin. Immediately after birth of the child there was a fairly profuse hemorrhage (500 c.c.). Repeated attempts to express the placenta were unsuccessful, and after one hour hemorrhage again became severe. Manual removal was decided upon and carried out. The procedure was made difficult by the presence of a moderate Bandl's ring which, however, relaxed under anesthesia. The placenta was firmly adherent to the uterus, and was removed only with great difficulty. Bleeding ceased and the uterus was firmly packed. The patient's condition was good, her blood pressure was 118/40. Pathologic examination of the placenta revealed no abnormalities in structure except for numerous infarcts. The intrauterine pack was removed in twelve hours, and there was no further bleeding. On the second day, 500 c.c. of blood were given to facilitate recovery. The patient was discharged after an afebrile hospital stay of ten days.

Six of the women investigated have not as yet become pregnant. Of these, 2 (33 per cent) desire pregnancy, but have remained sterile. Four are practicing voluntary contraception.

In total then, 6 of the 13 patients, or 46.15 per cent, show apparent after-effects of the manual removals performed on them, in terms of hemorrhage, abortion, or sterility.

CONCLUSIONS

1. Sixty-two cases of retained and adherent placenta with 54 manual removals have been presented.

2. The incidence of manual removal was 0.78 per cent, agreeing with the general average in the literature.

3. There was one maternal death, an uncorrected mortality of 1.78 per cent.

4. Fetal mortality occurred four times (6.6 per cent), twice in utero, and twice neonatally in premature infants.

5. Morbidity complicated the puerperium in 42 per cent of the cases, and was higher in the group of patients delivered by operative means.

6. The large number of elderly primiparas in this series adds another possible complication to the hazards of pregnancy in this age group.

7. The frequency of previous septic abortions and miscarriages adds strength to the concept of abnormal uterine status as a cause of adherent placenta.

8. Toxemia, pyelitis, and late post-partum hemorrhage were the most common prenatal complications.

9. Uterine inertia was an important complicating factor in labor which was prolonged in this series.

10. The most important immediate sequelae seem to be hemorrhage and sepsis.

11. The most common secondary sequelae seem to be sterility, abortion, and ante-partum hemorrhage in subsequent pregnancies.

We wish to thank Dr. M. W. Aaronson, Chief of Service, for his kind assistance. We are deeply grateful to Dr. M. A. Novey, Assistant Professor of Obstetrics, University of Maryland, for his invaluable aid in the composition of the manuscript.

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THE ROLE OF CESAREAN SECTION IN THE TOXEMIAS OF PREGNANCY*

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WITH the development of low cervical cesarean section in the past twenty years, there has been an increasing tendency toward combined medical and surgical treatment for toxemia of pregnancy. By this condition, we refer to that state characterized by the presence of at least two of the following symptoms: hyperpiesia, with a blood pressure of 140 systolic and 90 diastolic or higher; peripheral edema, and albuminuria, accompanied or not by a cardiovascular or renal component. In an attempt to evaluate the efficacy of this treatment, we made a study of the cesarean sections done for toxemia of pregnancy in the Michael Reese Hospital during the ten-year period of 1929 to 1939. We should like to preface our report by stating that in all cases the operation performed was a laparotrachelotomy, a procedure which has been in popu-

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lar use in this clinic for the past fifteen years because of its ease of performance, practicability, and safety.

No doubt the old classic section, under general anesthesia, had a higher mortality than medical treatment with pelvic delivery. It is possible that the laparotrachelotomy, under local anesthesia, has reduced the operative mortality to the extent that this operation may now be used more often. The results in the group of cases to be reported may tend to prove this likelihood. All the operations were done by eleven operators on both the private and the ward services. During this ten-year period, 681 cesarean sections were performed in a total of 15,555 deliveries, the indication being toxemia in 94. From 1922 to 1927 4 cesarean sections were done for toxemia, as compared with 57 in the following five years, 1927 to 1932.[1] The number of cesarean sections for toxemias from 1929 to 1939 varied from 6 to 15 a year, as shown in Table I.

TABLE I

YEAR	TOTAL NO. OF C. S.*	NO. OF PATIENTS WITH TOXEMIA	C. S. FOR TOXEMIA	% OF PATIENTS WITH TOXEMIA TREATED BY C. S.	% OF C. S. DONE FOR TOXEMIA
1929	72	59	15	25	21
1930	77	48	9	19	12
1931	67	40	6	15	10
1932	47	39	7	19	15
1933	39	37	6	16	20
1934	68	35	7	20	10
1935	59	40	8	20	14
1936	87	62	9	15	10
1937	89	51	13	26	15
1938	76	53	14	26	18
Total	681	464	94	20	14

*C. S., cesarean section.

INCIDENCE

Of 681 cesarean operations in this series, 94, or 14 per cent, were done for toxemia of pregnancy; 6 for eclampsia and the remaining 88 for pre-eclampsia and other allied toxemias. Hospital figures give the incidence of nonconvulsive toxemia of pregnancy in the United States as varying between 0.2 and 29 per cent, or an average of 4 per cent.[2] The incidence given by Allen in his discussion of the study of Dieckmann and Brown[2] was 6.2 per cent; and we found toxemia in 3 per cent of all admissions in the period under investigation, i.e., 464 cases of late toxemias in a total of 15,555 deliveries. In 94, or 20 per cent, of these cases, the pregnancy was terminated by cesarean section. Dieckmann and Brown[2] cited an incidence of cesarean operations of 16 per cent in the Chicago Lying-in series. Of the 94 patients in our series, 68, or 72 per cent, were primiparas, and 26, or 28 per cent, were multiparas. Delivery was premature at thirty-seven weeks or less in 52 cases, or 55 per cent of all the cases in which operation was performed.

MATERNAL MORTALITY

There was one maternal death in the group under study. The patient was a 40-year-old gravida iv, para iii, in her twenty-eighth week of pregnancy, who had severe pre-eclampsia, superimposed on chronic glomerulonephritis. She had made one prenatal visit before admission to the hospital. Her blood pressure on admission was 256 systolic and 160 diastolic, and she complained of irregular headaches and spots before the eyes. Significant laboratory findings were albuminuria 3-plus,

cylindruria 2-plus, and a nonprotein nitrogen content of the blood of 48 mg. per hundred cubic centimeters. The ocular findings were negative. The patient was placed under conservative management, including venesection with removal of 500 c.c. of blood. Four days after admission she continued to complain of severe headache and spots before the eyes. A bag induction was attempted but was not successful, after which a low cervical cesarean section was performed under ethylene anesthesia. On the fourth postoperative day, the patient showed signs of uremia and twitching, and the nonprotein nitrogen content of the blood was 62 mg. and the creatinine 2.9 mg., per hundred cubic centimeters of blood. The blood pressure at this time was 214 systolic and 140 diastolic. Forty-eight hours later the patient went into coma and died. This death accounted for our maternal mortality of 1.06 per cent.

TABLE II. CESAREAN SECTION FOR TOXEMIA

AUTHOR	MATERNAL MORTALITY PER CENT	FETAL MORTALITY PER CENT
Peterson, R.: J. Michigan M. Soc. 13: 4, 1914	35	None given
Holland, E.: J. Obst. & Gynaec. Brit. Emp. 38: 358, 1921.	31.8	46.9
Gordon, C. A.: AM. J. OBST. & GYNEC. 16: 307, 1928.	12.9	21.9
Tucker, S. B.: Texas State J. Med. 30: 591, 1935	6.25	6.25
Irving, F. S.: Canad. M. A. J. 40: 137, 1939	2.5	None given
Present series	1.06	13.5

A review of the literature (Table II), shows that with succeeding years the maternal mortality from cesarean section in cases of toxemia has been greatly reduced. We must bear in mind, of course, that this reduction has been due primarily to improved asepsis, increased surgical proficiency, and better obstetric judgment, as well as to a decided trend to low cervical cesarean section.

There was one nonoperative death due to toxemia of pregnancy. Including the death following cesarean section, the total maternal mortality was 0.43 per cent as compared with a 1.7 per cent maternal mortality in hospitals throughout the United States.

In the report of the United States Bureau of Census, it is stated that late toxemias of pregnancy cause annually 20 per cent of approximately 10,000 maternal deaths throughout the country. At the Michael Reese Hospital there were 35 maternal deaths in this ten-year period, 2, or 5.7 per cent, of which were of toxemic patients.

FETAL MORTALITY

It is generally agreed that the mortality of premature babies born of toxemic mothers is lower when these infants are delivered by cesarean section than by the vaginal route. It is especially true that toxemic babies do not tolerate labor well. There were 55 premature infants in the series, weighing between 900 and 2,500 Gm.; the remaining 41 infants weighed 2,500 Gm. or over. The gross fetal mortality was 13.5 per cent. The fetal mortality in infants weighing between 900 and 2,500

TABLE III. INCIDENCE OF VARIOUS TYPES OF TOXEMIAS

	NO. OF CASES	PER CENT OF CESAREAN SECTIONS
Pre-eclampsia	70	72.0
Eclampsia	6	6.3
Nephritic toxemia	8	8.5
Cardiovascular disease	3	3.2
Other toxemias	7	7.4
Total	94	

Gm. was 20 per cent; in those infants weighing above 2,500 Gm., it was significantly lower, 4.8 per cent. The fetal mortality in premature infants delivered vaginally has been given as about 47 per cent.[2] Table II shows the fetal mortality of cesarean section for toxemia.

INDICATIONS

Toxemia of pregnancy was the primary indication in all of these cesarean sections. Table III classifies the number and percentage of the various types of toxemias.

These cases represent both the private and the ward services of eleven operators. Most of the patients were hospitalized and given a thorough trial of conservative treatment. This treatment was quite uniform, consisting of sedation by the Stroganoff technique, absolute bed rest, restricted diet, purgation, and intravenous administration of dextrose; more recently magnesium sulfate has been used hypodermically or intravenously. The large percentage of patients subsequently operated upon represents cases in which, despite adequate medical management, the toxemia was progressive or stationary and the pregnancy thirty-two weeks or beyond, with the fetus viable. Low cervical cesarean section was performed in all these cases. Seventy-two per cent of the cesarean sections for toxemia were done on primiparas. The majority of multiparas have some dilatation, and if feasible, labor is induced and the patient delivered vaginally. Cesarean section is done on primiparas and multiparas in those cases in which the toxemia does not improve, the fetus is viable, and the cervix unripe for vaginal delivery. Local anesthesia was used in 40 per cent of the cases. The other anesthesias employed were induced by the following agents, named in the order of their frequency: ethylene, ethylene and ether, local anesthesia and ethylene, cyclopropane, and spinal anesthesia.

COMMENT

A combination of medical and surgical treatment was used in the cases of cesarean section for toxemia in this study. Dieckmann stated that cesarean section should be used only in the pre-eclamptic patient when eclampsia seems imminent and when delivery through the vagina seems unwise. We are of the opinion that it is an unnecessary risk to both the mother and the baby if the toxemia is allowed to reach a point where eclampsia is imminent, and that cesarean section should be performed at the earliest time consistent with the safety of the baby if the toxemia is progressive or does not improve in spite of hospital medical treatment. With the advent of low cervical cesarean section under local anesthesia and its low mortality, we think this procedure safer for the mother and the infant than awaiting the approach of eclampsia.

We also believe, as does Horner[2] that the sooner an unborn baby within the period of viability is separated from its toxemic mother, the better is its chance for life; and, conversely, the longer it is attached to its toxemic mother, the less likely it is to survive.

We agree with the statement from the American Committee on Maternal Welfare[3] that the long-continued toxemia of pregnancy is more productive of chronic arterial and renal disease than toxemia of short duration. We believe that if more of the patients in our study had been delivered vaginally, the maternal and fetal mortality would have been higher.

SUMMARY

1. A series of 94 cesarean sections done for toxemia of pregnancy at Michael Reese Hospital in the ten-year period from 1929 to 1939 is reported.

2. In the period under investigation, 5.7 per cent of all the maternal deaths were due to toxemia.

3. The maternal mortality in this study was 1.06 per cent.

4. The maternal mortality from all the toxemias of late pregnancy, including eclampsia, in the same period was 0.43 per cent.

5. The fetal mortality in the entire series was 13.5 per cent. The premature infant mortality was 20 per cent, and the mature infant mortality, 4.8 per cent. The mortality rate of premature infants delivered vaginally has been given as 47 per cent.

6. The incidence of cesarean section done for toxemia increased from 4, in five years from 1922 to 1927, to 94 in the ten-year period from 1929 to 1939.

7. Twenty per cent of the toxemic patients were delivered by cesarean section in this same ten-year period.

CONCLUSION

It is our impression that when the toxemia progresses, in spite of medical treatment, and the fetus is viable, it is more radical to carry the patient nearer to term in selected cases than to perform low cervical cesarean section. It would appear that the latter procedure carries a lower maternal and fetal mortality and alleviates undue strain on the cardiovascular-renal apparatus. Future studies may bear out this contention.

REFERENCES

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DISCUSSION

DR. WILLIAM J. DIECKMANN.—Excluding those cases where there is definite cephalopelvic disproportion, I believe cesarean section is occasionally indicated in the treatment of severe toxemia of pregnancy where either the patient has not been seen by a doctor or the doctor has adhered too long to medical management. Reports on the use of cesarean section in the treatment of eclampsia reveal that the maternal mortality ranges from two to 88 per cent.

According to Holmes, the mortality from cesarean section in the United States is 5 per cent. The average mortality for eclampsia is 13 per cent. Thus if the two conditions are present in the same patient, the mortality may be quite high. One reason for this high mortality is that the contraindications to cesarean section are not always recognized. In a period of nine years, 1,349 cesarean sections were performed in the Chicago Lying-in Hospital with an uncorrected maternal mortality of 0.67 per cent and a corrected one of 0.45 per cent. This low mortality rate has been achieved by recognizing that there are definite contraindications to laparotrachelotomy. This operation is not performed if the membranes have been ruptured over twenty-four hours; if the patient has been in labor over twenty-four hours; if attempts have been made to induce labor by some mechanical means; if forceps or version have been attempted; or if the patient's temperature is elevated.

Cesarean section is used in toxemic patients; (1) if there is cephalopelvic disproportion, (2) after medical treatment has been used in severe pre-eclamptic or eclamptic patients who are near term with a closed, uneffaced cervix, and (3) in patients with severe vascular or renal disease if termination is deemed necessary between thirty-two and thirty-eight weeks' gestation. Sterilization per se is not an indication. Cesarean section should not be used as a last resort.

The average mortality for eclampsia is 13 per cent and for nonconvulsive toxemia is 1.7 per cent. The patient who has not had convulsions is obviously a better risk than if convulsions once develop. Therefore, as Dr. Strauss has emphasized, it is much better to perform a cesarean section on the pre-eclamptic than on the eclamptic.

Seventeen per cent of 1,672 toxemia patients had the pregnancy terminated by laparotomy. Hysterotomies are included. In the period from 1931 to 1936, this figure was 21 per cent. In the next two years it was 14 per cent and in the period from 1938 to 1939 it was 9 per cent. Our incidence of hysterotomy and cesarean section in the treatment of pre-eclampsia is 11 per cent, in hypertensive disease 21 per cent, in nephrosclerosis 56 per cent and in glomerulonephritis 45 per cent. Eighteen per cent of 75 eclamptic patients had a cesarean section in our hospital. The decrease in the use of cesarean section is due to more intensive treatment of the ambulatory patient and earlier hospitalization if the toxemia does not respond to home management.

Over 20 per cent of our cesarean sections were performed for some other indication than toxemia. Forty-four per cent of the operations were in primiparas, a much lower figure than that reported by Dr. Strauss.

Eclampsia was present in 10 per cent, pre-eclampsia in 48 per cent, and vascular-renal disease in 13 per cent. In the multipara, pre-eclampsia was present in 10 per cent and vascular-renal disease in 49 per cent.

Dr. Strauss has stated that delivery through the vagina may increase the fetal mortality in toxemic patients. In general, our data, as well as those of Clifford from the Boston Lying-in, do not support this belief. The following data indicate that cesarean section is associated with a fetal mortality which is definitely higher than that associated with vaginal delivery. Of course, the number of severe toxemias is greater in the cesarean group, which would account for part of the increase in fetal mortality. There has been a steady decrease in our fetal mortality which we ascribe to the use of local anesthesia, the omission of all drugs which might interfere with fetal respiration, and the immediate transfer of the baby, if premature, to the Hess incubator.

The total fetal mortality for laparotomy was 17 per cent; for babies weighing over 1,000 Gm., 12 per cent; over 1,500 Gm., 11 per cent; and over 2,500 Gm., 6 per cent. The fetal mortality for babies weighing over 1,500 Gm. for the period from 1931 to 1936 was 12 per cent and for the next three years was 4, 4, and 3 per cent, respectively. Fetal mortality is also dependent on the type of maternal disease. Thus, in mild toxemia, fetal mortality is 7 per cent, in severe pre-eclampsia 17 per cent, in severe hypertensive disease 27 per cent, in nephrosclerosis 39 per cent and in glomerulonephritis 58 per cent.

Dr. Strauss has stated that long-continued toxemia is likely to be followed by chronic vascular-renal disease. I take exception to this statement. It is my experience that a patient with severe pre-eclampsia cannot be carried for weeks. If such a patient can be carried for a period of several weeks, the condition is one of hypertensive disease and obviously such a patient may have a persistent hypertension after delivery or a recurrence of the toxemia in a subsequent pregnancy.

DR. W. H. RUBOVITS.—There is an occasional toxemic patient in whom the conditions are quite ideal for the performance of vaginal cesarean section, especially in a multipara with roomy pelvis and relaxed tissue.

Another point to consider is the advisability of performing a section even though the patient has already developed convulsions. If the convulsion has been mild or easily controlled and a number of hours have elapsed without evidence of the appearance of more convulsions, I think that we should not be deterred by the rule which has been adopted in many clinics that a patient once having developed convulsions should not be sectioned.

DR. FREDERICK H. FALLS.—Dr. Strauss voices pretty much the same opinion that I stressed in 1935 when I reported my first 500 cases of eclamptic toxemia. At that time I admitted that I was heretic in suggesting cesarean section in a large percentage of eclamptic patients, because the overwhelming opinion then as now was against this procedure.

In our clinic we believe that if this convulsive type appears as a fulminating, rapidly advancing toxemia that immediate cesarean section is the safest way out for mother and baby. Those patients who have the slightest evidence of advancing toxemia that is not controlled by dietary advice on home management are immediately hospitalized and put under strict medical management, and then if they do not improve we deliver by medical or mechanical induction of labor or cesarean section as best suits the case.

We use local anesthesia on all the nonconvulsive types, but not on the convulsive type, because we feel that a general anesthesia prevents convulsions while we are operating, which avoids many undesirable complications.

We do not believe that there is a great deal of evidence of improvement in statistics due to low cervical section as far as our experience goes. The group in which we have done low cervical section has about the same mortality as the group in which we have done the classical section. We have now something over 70 eclamptic toxemic patients who have been delivered by cesarean section, every other one a low cervical and every other one a classical. These cases were done in the same operating room with the same nursing personnel, the same doctor, and the same technique, and we got about the same results.

The rule in my clinic is that we never do cesarean section on eclamptic patients if we can avoid it. We do it in all cases in which we feel the danger of allowing the patient to go further in pregnancy is greater than the danger of doing the operation. The greatest danger is in procrastination, in trying to get the obstetrician to make up his mind, that there is an indication present that will be defensible if he does a cesarean section and loses the case. We have had fewer deaths in the patients operated upon, convulsive and nonconvulsive, than in those treated conservatively.

AN ELEVEN-YEAR SURVEY OF CESAREAN SECTION AT A SMALL COMMUNITY HOSPITAL

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THIS study of cesarean sections performed at the Mount Vernon Hospital is presented not with the intention of illustrating inferiority or excellence of results obtained, but rather to further the thought that in order to evaluate properly the status of abdominal section, considerably more attention must be paid to the preparing and publishing of such surveys from smaller hospitals.

The surveys and statistical results obtained from the leading obstetric clinics are well publicized, appreciated, and duly admired. They represent the par for the course. Excellently staffed, well-equipped, and with all decisions and techniques under the direct control of obstetric specialists, it is only reasonable to expect superlative results. However, the bulk of obstetric practice does not take place in these leading centers. It is largely entrusted to the hands of the small, moderate-sized voluntary and community general hospital, wherein every general practitioner does his "confinement work" and thereby directly influences the incidence, type morbidity, and mortality of abdominal delivery.

This survey represents the eleven-year study of cesarean section in such a 200-bed community hospital in which fifty-odd general practitioners "do obstetrics" and when in trouble call upon the services of several surgeons or obstetricians to help them out. This situation un-

doubtedly more truly represents nation-wide conditions. If real improvement in morbidity statistics is to be made, it must, in the final analysis, be obtained by bettering the results of this great group of smaller hospitals. The making and publishing of small hospital surveys will stimulate local interest and community rivalry and will inevitably reflect improvement in end results. To illustrate this point: In 1935, the first five-year survey of sections performed in this hospital was presented to the staff. It showed the appalling mortality rate of 10 per cent. In 1940, the second five-year survey was likewise prepared and reported. It showed the pleasing reduction in mortality to 3.7 per cent. Can anyone gainsay that the critical analysis in 1935 did not at least have a part in achieving this improvement?[7]

STATISTICAL ANALYSIS

In period I, the section incidence was 2.1 per cent. In period II, the incidence was 3.1 per cent. For the entire eleven-year period, there were 8,459 deliveries with 204 sections, which is an incidence percentage of 2.6, a fairly conservative figure.

TABLE I. INCIDENCE OF SECTION

PERIOD I. 1930-1935			PERIOD II. 1936-1940		
YEAR	BIRTHS	SECTIONS	YEAR	BIRTHS	SECTIONS
1930	822	19	1936	689	22
1931	823	15	1937	781	17
1932	790	17	1938	752	23
1933	746	14	1939	831	23
1934	635	13	1940	830	22
1935	662	19			
Total	4,478	97		3,883	107

TABLE II. INDICATIONS

	PERIOD I 1930-1935	PERIOD II 1936-1940
Contracted pelvis, before labor, elective	6	15
Dystocia, cephalopelvic disproportion	34	33
Pre-eclampsia	0	4
Eclampsia	16	4
Abruptio placentae, accidental hemorrhage	3	6
Placenta previa	9	13
Repeat section	14	12
Cardiac	4	3
Previous operative repair	3	3
Fibromyoma	4	4
Pulmonary hemorrhage	1	0
Sterilization	1	0
Interest of child	2	9
Chorea of pregnancy	0	1
Total	97	107

Table II presents a comparison of the indications for abdominal delivery in the two series. Several observations are pertinent.

Notwithstanding the availability of x-ray pelvimetry, it is apparently still very difficult for the general practitioner to evaluate properly comparative cephalopelvic proportions. In the two series, there is but little improvement in the number of elective sections for disproportion. Trial of labor was resorted to in the majority of

disproportions. In justification, may it be said that proper evaluation of a pelvis is still the most difficult task which confronts the trained obstetrician, not to mention the lack of uterine force and the deficiency of mental and physical stamina with which so many of our modern women approach labor.

It is gratifying to note the marked reduction in sections for eclampsia from 16 per cent in the first group to 4 per cent in the second group.

The hemorrhagic complications of pregnancy were treated by section in both series. This is quite in accord with the best-informed opinion of today.

The smaller number of repeat sections in both groups is striking. Undoubtedly the economic factors attending the depression decade with its marked increase in elderly primiparas has precluded further pregnancy in this group.

The group of sections done primarily in the interest of the child shows a marked increase in the second series. As the typical American family shrinks in size, the value of each baby proportionately increases. The elderly primigravida with breech presentation or the sterility problem which has finally become pregnant after much expense is not in a mood to gamble with the safety of the child when confronted with the possibility of its loss.

TABLE III. COMPARATIVE INDICATION STATISTICS

INDICATIONS	MOUNT VERNON, N. Y. 8,459 DELIVERIES 204 SECTIONS, 2.6%	CHICAGO LYING-IN 18,000 DELIVERIES 1,000 SECTIONS, 5.5%
Disproportions and dystocia	44.0%	47.0%
Placenta previa	10.6%	7.9%
Abruptio placentae	4.3%	4.6%
Eclampsia	9.6%	0.9%
Pre-eclampsia	1.9%	6.5%
Repeat section	8.0%	28.0%

Table III gives a comparative analysis of the indications at our hospital and those of a large obstetric center. The marked disparity in the figures for eclampsia is obvious. The tendency is the first series was to operate during the stage of convulsions. In the second series, we too learned but apparently not enough to treat the eclampsia medically when fully developed. We are also learning that section may be the very best way of treating pre-eclampsia, particularly in the untried pelvis. The striking difference in repeat sections is noteworthy. This, of course, contributes to the larger cesarean percentage figures for the obstetric center and by dilution with clean, uninfected cases improves the morbidity statistics for the larger center.

TABLE IV. TECHNIQUE USED

TYPE OF OPERATION	GROUP I 1930-1935 97 SECTIONS	GROUP II 1936-1940 107 SECTIONS
High classic	31%	15.0%
Low classic	36%	25.0%
Double flap	25%	49.0%
Porro	0	4.5%
Latzko	1%	2.0%
Broadhead exclusion	4%	0
Froste-Smith extraperitoneal	0	4.0%

Table IV shows the various types of operations used in the two periods. In Period I, 67 per cent of all sections were of the classic type and but 25 per cent were of the double flap or low segment type. In Period II, only 40 per cent were of the classic type while 50 per cent were of the double flap variety. In addition, 4 per cent of the cases were hysterectomized and 6 per cent were of the extraperitoneal type. In other words, the staff became definitely infection-conscious and progressive attempt was made to preclude peritoneal contamination and infection by getting down into the

lower uterine segment, by removing the uterus or by excluding the uterine incision from the peritoneal cavity. The significance of this change in technique will be evident in the mortality tables.

TABLE V. COMPLICATIONS FOR PERIOD II, 107 SECTIONS

COMPLICATIONS	1936-1940 NO. CASES	1936-1940 PER CENT
Phlebitis	7	9.0
Embolism	3	2.9
Atelectasis pneumonia	7	9.0
Wound infection	5	4.8
Shock or hemorrhage	14	12.0
Ileus	5	4.8
Retained placenta	3	2.8
Disruption previous scar	2	1.9
Peritonitis	3	2.8

Phlebitis.—This occurred three times as frequently in the cases wherein trial of labor was resorted to.

Embolism.—All were pulmonary in type. There were two recoveries and one fatality on the twenty-seventh postoperative day. Two of these cases were clean, elective cases. The fatal case was the only one showing clinical evidence of thrombophlebitis.

Atelectasis and Pneumonia.—Fortunately, there were no fatalities in the group. Twelve per cent of nonelective cases showed pulmonary signs, whereas only 4 per cent of the elective were similarly affected.

Wound Infection.—All occurred in cases with ruptured membranes and 3 out of the 5 cases were drained at the time of operation on the suspicion of infection already present.

Shock and Hemorrhage.—Ten cases showed evidence of moderate shock or hemorrhage postoperatively, whereas 4 cases showed marked shock or hemorrhage. Of these latter, two were complete placenta previas with marked preoperative blood loss, one was a total eclamptic with marked blood loss on the table, and one suffered severe hemorrhage when uterine incision extended through uterine vessels and into vaginal plexus. No fatalities from shock or hemorrhage occurred in this five-year period under consideration. Ninety cases out of 107 were typed before operation and 44 received one or more transfusions. Nearly all received intravenous glucose at the table or on return to their room. This careful attention in preparation for the prevention and early treatment of shock or hemorrhage has greatly improved the results obtained in the first period. At the present time, it is practically routine in this hospital not to begin cesarean operations until a compatible donor is in the hospital.

Ileus.—With the exception of the peritonitis cases, ileus was not a prominent finding in this series of cases. It was only severe in two high classic cases and here was quickly controlled by the Wangensteen suction drainage. The diminution in ileus and distention is undoubtedly due to the advantages gained by the low cervical incision and the routine use of prostigmin or pitressin immediately postoperatively.

Retained Placenta, Lochiametra.—It is of interest to note that abdominal section does not preclude the possibility of retained secundines. These patients bled postoperatively and suffered temperatures up to 104° F. Relief occurred when placental tissue was passed or removed through the cervix. Greater attention would have saved this complication.

Disruption of Previous Cesarean Scar.—In two repeat sections, the previous uterine scar had separated so that only the membranes kept the baby from the peritoneal cavity. Both of these patients had been previously sectioned for eclampsia by the classic routine, and both were extremely edematous at the time of that section. This may have been a factor in the poor healing of their incisions. Inasmuch as 2 out of 12 repeat sections showed disrupted scars, we feel that decision to deliver per vaginam after previous section is not to be taken too lightly.

Peritonitis.—All 3 cases ended fatally. All had ruptured membranes and all had been examined vaginally two or more times. One was a classic for partial placenta previa and two were low flaps for dystocia with membranes ruptured for many hours.

Although the low flap operation limits infection in the potentially unclean cases, it apparently is not a preventive for the initial spill in the grossly infected case. Its indication must not be pushed too far. In actually infected cases nothing short of a true extraperitoneal approach should be elected. In this series of 204 sections, 11 true extraperitoneal sections for frankly infected cases suffered no mortality.

Table VI shows the cause of death. In the first period, there were four deaths from shock or hemorrhage. The indications, respectively, were (a) unrecognized rupture of uterus (repeat section-patient allowed to go into labor during night while awaiting elective section following morning), (b) eclampsia operated during convulsion stage without preliminary treatment, (c) central placenta previa uncontrolled by packing, and (d) very prolonged labor. All of these were sectioned by the classic route. Only one had been typed preoperatively and none were transfused in time to prevent death. In the second period, there were no deaths from shock or hemorrhage.

TABLE VI. MATERNAL MORTALITY

CAUSE OF DEATH	PERIOD I	PERIOD II
Shock or hemorrhage	4	0
Peritonitis	5	3
Embolism	0	1
Number of deaths	9	4
Number of cases	97	107
Percentage mortality	10	3.7

In the first period, there were 5 deaths from peritonitis. All had ruptured membranes. All were sectioned by the classic route for dystocia after varying lengths of trial labor. One was further complicated by eclampsia. In this first series, 5 out of 34 patients sectioned for dystocia after rupture of membranes and trial labor died of peritonitis. Strangely enough, in the second period this appalling mortality was not greatly changed. There were 3 deaths out of 33 similar disproportion cases although two were sectioned by the double flap method. It is, therefore, apparent that in this hospital at least any transperitoneal section for dystocia with ruptured membranes and trial of labor carries with it a high mortality rate.

Table VII shows the mortality according to the type of operation used. The figures are too obvious to need much comment. It is, however, true that the less qualified surgeon elects the classic route because of ease of accomplishment and, therefore, puts that operation under the added handicap of his inexperience. On the other hand, it is also true that the suspected infected cases are usually done by the double flap method which should, to a large extent, counterbalance this factor. The case for the true extraperitoneal approach in the slightly infected problem looms larger and larger and will undoubtedly supplant the low cervical section for this type of case.

TABLE VII. MATERNAL MORTALITY

TYPE OF OPERATION	NO. CASES	DEATHS	PER CENT
High classic	46	6	13.0
Low classic	51	4	7.8
Double flap	75	3	4.0
Extraperitoneal	11	0	0
Porro	6	0	0

Table VIII reveals the par toward which smaller hospitals must strive. The statistics of the large obstetric clinics are admirable. In all fairness, it must be realized that the dilution caused by the large number of repeat sections (28 per cent of clean, elective cases) contributes to the excellence of their final statistics. The mortality at Mount Vernon Hospital for the past five years has dropped to 3.7 per cent and with no fatality for the last 50 cases.

TABLE VIII. COMPARATIVE MORTALITY STATISTICS

SOURCE	NO. DELIVERIES	NO. SECTIONS	PER CENT OF SECTIONS	PER CENT OF MATERNAL MORTALITY
National before 1931	262,852	2,289	0.77	9.45
National 1931-1939	782,718	15,768	2.55	4.69
Chicago Lying-in 1930-1939	18,009	1,000	5.5	0.8
New York Lying-in	5,456	153	2.8	0.65
Mount Vernon, New York	8,459	204	2.6	5.1

TABLE IX. FETAL MORTALITY, 1936-1940

Deaths—10 9%

Stillborn

(a) 5 pound premature with abruptio placentae and Porro
(b) 3 pound premature in fulminating eclampsia

Neonatal—8

(a) Three monsters, anencephaly with megalofetus, breech with hydrocephaly, congenital heart with absence of abdominal wall.
(b) Two prematures with placenta previa
(c) Two atelectatic aspiration pneumonias
(d) One premature in nephritic mother

Table IX reviews the fetal mortality. In the hemorrhagic and toxemic group, the life of the mother was at stake and section was elected in spite of the evident prematurity of the fetus. The aspiration deaths were probably preventable. We have, in recent months, instituted a definite resuscitation team. The two monster deaths were due to error in judgment. Both sections were done in the interest of the fetus. The fetal heart was irregular before labor, and it was assumed that there was cord compression. The irregularity proved to be due to congenital anomaly and not due to fetal distress.

SUMMARY

It is felt that any evaluation of the status of cesarean section is incomplete without the inclusion of statistics from the smaller community hospitals. Such a survey has herein been presented. It is likewise felt that it is more truly representative of general conditions than the surveys from the larger and leading obstetric centers. It is hoped that the natural local rivalry instigated by the publication of such surveys will inevitably tend to produce better results.

CONCLUSIONS

The most common causes of death in cesarean section still are peritonitis, shock, and hemorrhage. The treatment of dystocia after rupture of the membranes and trial labor by any form of transperitoneal section carries with it considerable risk. The low cervical section is a vast improvement over the older classic methods and will, undoubtedly,

lower morbidity and mortality figures in the potentially infected cases, but its indications can be and are pushed far beyond the limits of safety. The true extraperitoneal approach should and will supplant the low cervical section in this type of case.

The general surgeon or obstetrician who cannot bring to the operating table the skill and judgment necessary to perform the various types of extraperitoneal section carries a distinct hazard to his hospital and should be excluded from this particular branch of surgery.

The general practitioner or general surgeon with little or no obstetric training is not particularly qualified to evaluate the dystotic pelvis. All decisions to perform such operations should be made in consultation with a skilled obstetric specialist.

The obstetrician who does not adequately prepare in advance for the eventuality of shock and hemorrhage in cesarean section likewise contributes to the too high mortality for this operation.

Finally, the general practitioner, who does not approach each obstetric problem with respect and with the thought of possible abdominal delivery and who by needless interference and haphazard judgment jeopardizes the safety of that operation, has likewise been remiss in his duty to his patient.

A METHOD FOR REDUCING THE SIZE OF THE UTERUS IN VAGINAL HYSTERECTOMY*

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VAGINAL hysterectomy may be performed by any one of many techniques. A large uterus is usually reduced in size by splitting in two or by morcellation and then removing it piecemeal. In the course of these procedures, it was found that amputating the cervix facilitated the turning of the corpus. Also in a large corpus (i.e., multiple fibroids), it was found that a good part of the corpus could be coned out with the cervix. However, there was the danger of opening an infected cervix or opening the uterine cavity in which a carcinoma might be present. Since carcinoma of the corpus or isthmus of the uterus may be associated with fibroids (0.5 to 4.4 per cent, according to different observers; 10 per cent over the age of 50 according to Bland-Sutton), I developed a procedure to decrease the size of the uterus without opening the cervical canal or the cavity of the corpus. The new procedure is helpful not only for a large uterus but also for carcinoma of the corpus or isthmus associated with fibroids and in unsuspected chronic pyometra secondary to stricture of the cervix.

In a consideration of the technique of vaginal hysterectomy, it is of interest to relate its historical development. No mention of vaginal hysterectomy was made in

*Presented at a meeting of the Chicago Gynecological Society, March 21, 1941.

ancient gynecology until the time of Soranus who practiced in Rome from A.D. 98 to 138. He suggested that if part or all of the uterus became black, because it remained prolapsed for a considerable time, it should be resected partially or entirely. Paulus Aegineta (A.D. 625 to 696), who appeared to be the first professional man midwife, advocated the operation for irreducible inversion. The next reference to the operation was for ulcerated prolapse by Albucasias the Arabian (1073 to 1106). No details of the procedures were given. There is no mention of it during the Renaissance.

In the modern period, Andreas A. Cruce, of Granada, performed a hysterectomy in 1560 with a cautery iron for a carcinoma in a prolapsed uterus. This method was used for the treatment of carcinoma of the cervix for quite some time. In 1813 C. J. M. Langenbeck performed a vaginal hysterectomy by enucleating a carcinomatous prolapsed uterus without opening the peritoneum. Langenbeck published the first monograph on the subject in 1818. Following this work came Sauter's description of dividing the broad ligaments and performing a vaginal hysterectomy in 1822. Blundell in 1828 and Recamier in 1829 published their experiences. J. C. Warren in 1829 apparently did the first vaginal hysterectomy in America. Many failures followed, probably due to imperfect asepsis and lack of anesthetics. Only few cases were found in the literature until W. A. Freund in 1878 described his technique for vaginal hysterectomy. Freund's technique is still practiced today and has served as the basis for all modifications of vaginal hysterectomy. Czerny, Liebman, Hegar, Kaltenbach, and Martin played an important part in developing the earlier technique. In the present century Kelly, Schuchardt, Schauta, Adler, and their followers are the main exponents. Doyen (1859-1916) who performed the operation by the use of clamps said, "No man can call himself a gynecologist until he can perform a vaginal hysterectomy," and "that the gynecologist shall be capable of applying as faultless a technique per vaginam as he would if performing per abdomen." Today Kennedy, of Philadelphia, still champions the clamp method advocated by Price.

AUTHOR'S TECHNIQUE OF VAGINAL HYSTERECTOMY

1. Usual preoperative preparation of 1 per cent iodine douche and soapsuds enema night before and morning of operation.

2. Morphine ($\frac{1}{6}$ gr.) and scopolamine ($\frac{1}{150}$ gr.) one and one-half hours and three-quarters of an hour before operation if no change in pulse (above 120) and respiration (below 12).

3. Anesthesia: ether, ethylene, cyclopropane or local (pudendal block and infiltration 1 per cent novocaine).

4. Lithotomy position; vaginal preparation of soap and water wash, iodinization and catheterization. Buttocks four to six inches over edge of table.

5. Weighted speculum inserted into the vagina. Cervix grasped with two vulsella and firmly pulled down. Lateral retraction. 2.0 c.c. of pituitrin (S) injected into the cervix.

6. Circular incision around portio guided by estimate of position of bladder and depth of posterior cul-de-sac. Vaginal wall wiped back with gauze exposing anterior and posterior peritoneal reflections.

7. Posterior peritoneal sac is opened between uterosacral ligaments and sutured to the vaginal wall with three fine (0) catgut sutures which are kept long on a Kocher forceps (Fig. 1).

8. Each uterosacral and part of the paracervical ligaments are clamped, cut, and ligated (No. 2 chromic catgut), and then sutured into the adjacent vaginal wall (Fig. 2).

9. Anterior peritoneal sac is opened between bladder pillars and the edge is sutured to the vaginal wall with three fine (0) catgut sutures

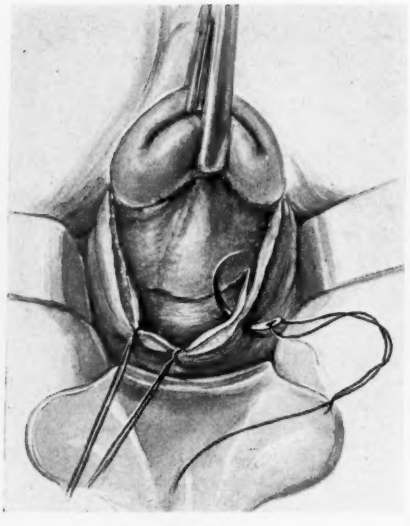

Fig. 1.

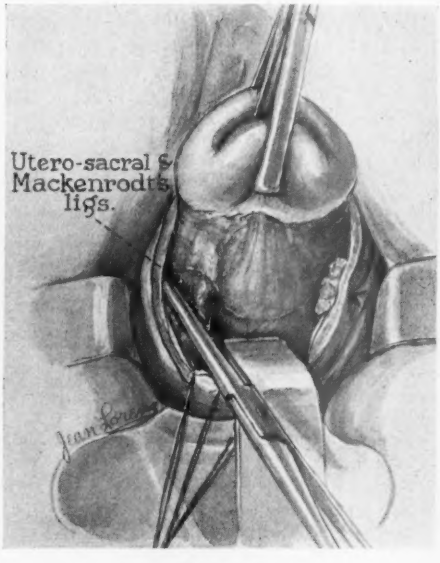

Fig. 2.

Fig. 1.—Modified vaginal hysterectomy: Posterior cul-de-sac has been opened and the posterior peritoneum is sutured to the posterior vaginal wall. The same procedure is carried out anteriorly, so that the anterior peritoneum is sutured to the anterior vaginal wall.

Fig. 2.—Modified vaginal hysterectomy: The uterosacral and the base of the Mackenrodt's ligaments are clamped, cut, and sutured to the lateral wall of the vaginal vault on each side.

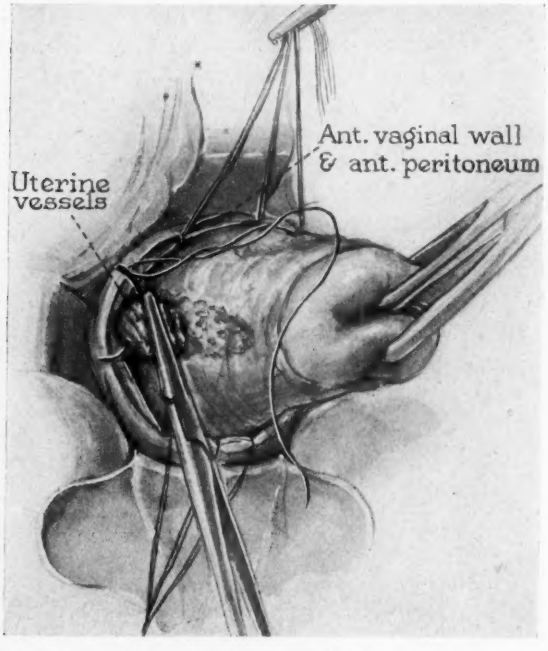

Fig. 3.—Modified vaginal hysterectomy: The bladder is retracted as well as the posterior peritoneum. The uterine vessels are clamped, cut, and ligated.

which are held long by a Kocher forceps. A long narrow retractor raises the bladder.

10. The uterine vessels are visualized, clamped, cut, and ligated on each side (No. 1 or 2 chromic catgut). A long narrow retractor is inserted into the posterior cul-de-sac (Fig. 3).

11. An incision is started in the uterine wall just medially to the right uterine vessels and continued toward the left side and carried around. As the cervix is pulled down, the myometrium is cut so that the whole endometrial cavity with a thick layer of myometrium is removed with the cervix. Only the tubal lumina are traversed (Fig. 4).

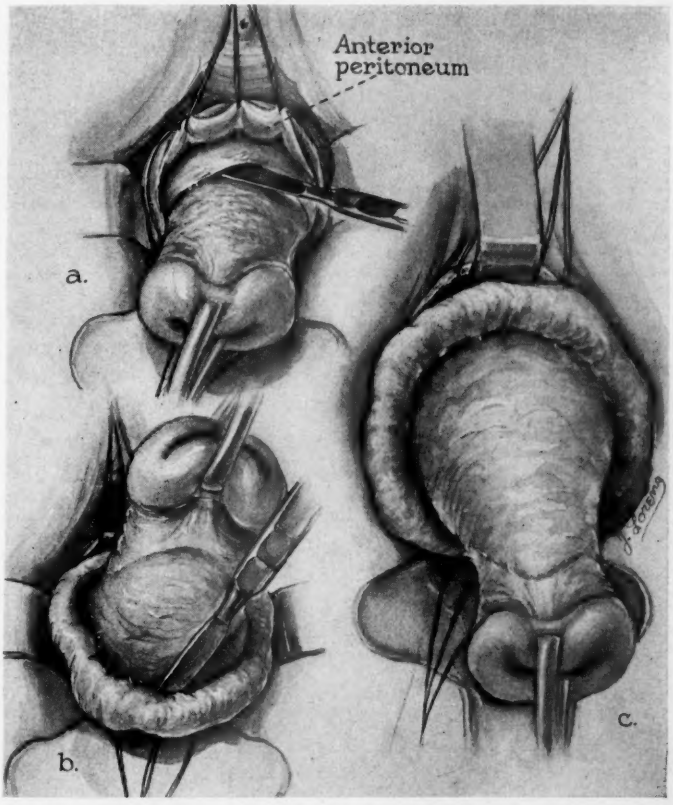

Fig. 4.—Modified vaginal hysterectomy: (a) The incision is now started medially to the point where the vessels have been ligated and encircles the cervix. (b) The cervix is pulled firmly downward and then upward as the major portion of the myometrium is shelled-out, leaving a capsule. (c) The major portion of the myometrium with its unopened endometrial cavity comes away.

12. The fundus is brought forward through the anterior cul-de-sac (Fig. 5), or if there are many fibroids, morcellation may be necessary. The round ligaments, tubes, and uteroovarian ligaments on both sides are clamped, cut and ligated with long No. 2 chromic catgut sutures which are held. The fundus is thus removed. The adnexa are inspected for possible pathology. The uterine and cervical cavities are opened by an interne or an unscrubbed nurse to allow the operator to inspect

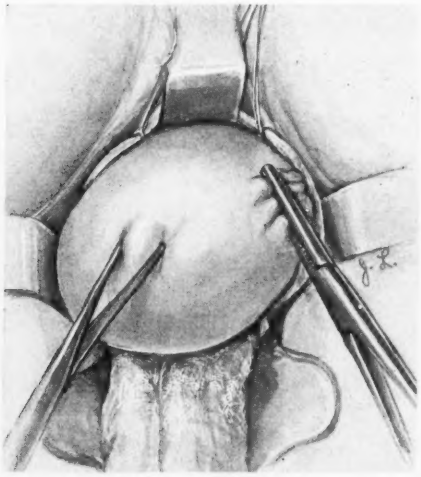

Fig. 5.—Modified vaginal hysterectomy: The remaining capsule of myometrium is brought forward exposing the tube, the round and uteroovarian ligaments, which are clamped on each side; the fundal capsule is removed; the tubes and ovaries are inspected. The uterine and cervical cavities are exposed by another person and the operator then inspects the cavities for carcinoma as the specimen is held up for his observation. If no carcinoma is found, the ligament stumps are ligated.

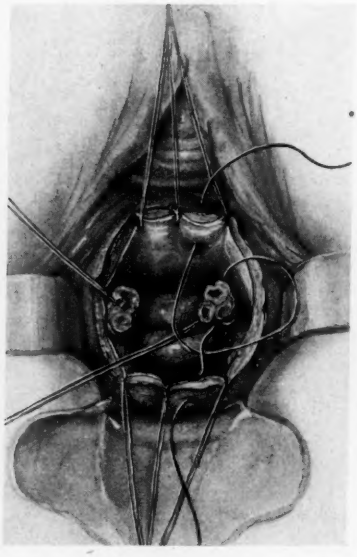

Fig. 6.

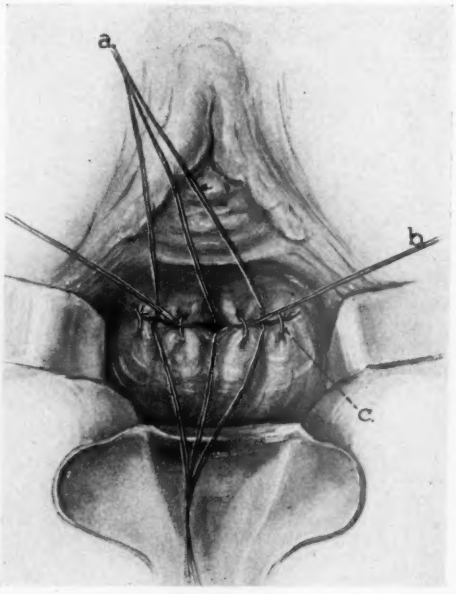

Fig. 7.

Fig. 6.—Modified vaginal hysterectomy: The ligament stumps are fixed in the midline of the vaginal vault, allowing only a small space between them. The stumps are, therefore, extraperitoneal, pulling up and supporting the central portion of the vagina and in most instances lengthening the vagina.

Fig. 7.—Modified vaginal hysterectomy: The lateral portions of the vault are closed with interrupted sutures. An iodoform gauze drain is inserted in the central opening of the vault. All sutures are now cut.

the endometrium. If carcinoma is present, the adnexa are excised by clamping the infundibulopelvic ligament, cutting, and ligating. The round ligaments alone are then utilized for fixation into the vaginal vault. If there is no carcinoma in the uterus or pathology in the adnexa each tube with its broad ligament, the round and uteroovarian ligaments are ligated (No. 2 chromic catgut).

13. The anterior vaginal wall with its peritoneum is sutured to the posterior wall with its peritoneum including the ligaments (Fig. 6). The lateral parts of the vaginal wall are sutured with one or two interrupted No. 1 chromic catgut suture. Thus, the ligaments and vessel stumps are extraperitoneal (Fig. 7). An iodoform gauze is inserted partly into the small peritoneal opening between the ligament stumps. The gauze is allowed to remain in place for forty-eight hours.

14. Any anterior or posterior plastic repair may now be done in the usual way.

POSTOPERATIVE CARE

1. One thousand cubic centimeters of 10 per cent glucose in normal saline solution intravenously.

2. Morphine sulfate, ⅙ gr. as necessary for forty-eight hours, then codeine sulfate and luminal for pain.

3. Fluids after nausea.

4. Catheterize every eight hours, or if patient urinates in small amounts, catheterize for residual urine every twelve hours.

5. Soft diet on second day and then solid food is added as indicated. Oil retention enema on third night followed by warm tap water enema the following morning. Mineral oil is given twice a day.

6. Patient is out of bed on the eighth day, walks on the ninth and may go home on tenth or twelfth day.

COMPLICATIONS

Low grade infections in the vault of the vagina as indicated by fever and foul seropurulent vaginal discharge have been observed which have responded to low pressure antiseptic douches. No marked infection such as peritonitis or pelvic abscess and no postoperative hemorrhages either immediate or late have been observed. In the subsequent postoperative examination granulation tissue in the wound or rarely a prolapsed fimbriated end of a tube have been seen.

The advantages of vaginal hysterectomy are: First, less shock, because of less exposure of the peritoneal cavity, and shorter operating time; second, no opening or closing of the abdominal wall, especially in an obese individual; third, no abdominal scar with risk of ventral postoperative hernia or evisceration; fourth, opportunity to overcome cystocele, rectocele, or enterocele; fifth, postoperative care is simple; sixth, drainage is better; seventh, convalescence is rapid and, therefore, shorter hospitalization. The contraindications are: First, fixation of the uterus due to large fibroids (larger than twelve weeks' pregnancy); second, pelvic inflammatory disease or previous pelvic operations; third, malignant disease of the corpus uteri in nullipara; and fourth, necessity for abdominal exploration.

The technique described by me adds to the advantages of vaginal hysterectomy by enabling one to remove large uteri, by preventing contamination of the peritoneal cavity, and by avoiding the spill of carcinomatous tissue from an unsuspected carcinoma of the uterus.

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DISCUSSION

DR. N. SPROAT HEANEY.—In the case described in the film, this procedure seemed to facilitate the hysterectomy greatly as the operator was enabled thereby to exert continuous traction and remove the uterus more rapidly than if the usual technique of morcellation had been followed. For this purpose I believe that his method is of distinct advantage. I do not believe that it is of importance in avoiding contamination from a carcinomatous or infected endometrium, particularly in view of the fact that he did not exercise the common precaution of blocking the cervical canal by sutures or clamps to prevent a spill through the cervical opening. Pulling down continuously as he did, increases the chance of escape of any infected material that may be in the uterine cavity, through the cervical canal. I wonder how often Dr. Lash is able to remove a block of the uterus containing the endometrial cavity without entering the endometrial cavity, since in fibroids of any size the uterine cavity is so tortuous that its location cannot be determined.

DR. H. O. JONES.—Dr. Lash removes the endometrial cavity but he leaves a certain amount of endometrial tissue between the Fallopian tube and the cavity of the uterus. As we know from Sampson's work this tissue has a proliferative activity, and it seems to me that it would be very dangerous to leave that portion of the Fallopian tube in.

Like Dr. Heaney, I cannot see any advantage and I can see many disadvantages in the use of this procedure.

DR. FREDERICK H. FALLS.—Dr. Lash has not pointed out that a similar operation of this kind may save difficulty in certain vaginal hysterectomies which cannot be done in a routine manner because of certain complications which preceded the indication for the operation, such as pelvic inflammatory disease. We have done a number of operations with a technique similar to that described by Dr. Lash in patients who had had an interposition operation and in whom the uterus had begun to show fibroid or malignant degeneration. One of our chief concerns is to remove the uterus without injury to the bladder. We take out practically all of the myometrium and do an extraperitoneal vaginal hysterectomy. In another group of patients which special indications created we have done vaginal hysterectomies on uteri that have had previous ventral suspensions. We have used this same technique Dr. Lash has shown and then left a small portion attached to the abdominal wall.

To avoid contamination, instead of sewing the cervix we pull it down and with a cautery cook the interior of the uterus. By doing that we thoroughly sterilize the cavity of the uterus, and then we can do what we want with the uterus. I do not think it is good technique to put iodoform gauze through the cervix of the uterus.

DR. W. H. RUBOVITS.—I can see some definite advantages in the operation that Dr. Lash performs. There is a definite advantage to reducing the size of the large uterus which we formerly did, either by splitting the uterus in the midline and removing one-half of the uterus at a time or by some form of morcellation. I can see no better way than the operation Dr. Lash describes of cutting away a

large portion of the uterus through the avascular area which will remove the endometrial cavity and a large block of the fibroid uterus.

DR. LASH (closing).—The suggestion of closing the cervix is an excellent one. I have tried to avoid the necessity of that by putting iodized gauze into the canal and using a volsellum. I do not use this operation in an infantile uterus, but in a large uterus. Whenever it is possible, the uterus is removed intact.

The reason we took out this uterus in the illustrated case, was that the patient, a 44-year-old woman, was bleeding and had multiple fibroids and large cystic ovaries.

It is true that we have to traverse the tubal cavity in removing the endometrial cavity, but we try to get the major portion of the myometrium in removing the myometrium with the endometrium. Two cubic centimeters of pituitrin will make the myometrium practically bloodless.

I would like to reiterate that this operation is not to be done on the normal uterus where the corpus can be removed in toto. It is the uterus the size of a twelve to fourteen weeks' pregnancy that should be removed this way. In certain instances, as Dr. Falls brought out, we can really remove the uterus in the presence of inflammatory disease where there are some adhesions present.

DISTURBANCES IN PREGNANCY AND LABOR IN GUINEA PIGS WITH HYPOTHALAMIC LESIONS*

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(From the Institute of Neurology, Northwestern University Medical School)

GONADOTROPIC hormones formed in the anterior lobe of the hypophysis are essential factors in the development of the Graafian follicles, in ovulation and in corpus luteum formation. Ovarian hormones in turn react upon the anterior pituitary. Without a proper balance of the pituitary follicle-stimulating and luteinizing hormones and the ovarian estrogenic and corpus luteum hormones pregnancy cannot occur. It is possible that the hypophysis may also influence pregnancy through its thyrotropic hormone and the thyroid gland. There is some evidence that the oxytocic hormone formed by the posterior lobe of the hypophysis may play a role in normal labor (Fisher, Magoun and Ranson, 1938).

The master gland, the hypophysis, lies close to the base of the brain to which it is attached by the infundibulum. The part of the brain to which it is attached is known as the hypothalamus. It forms the floor of the third ventricle immediately behind the optic chiasma. In recent years evidence has accumulated to show that the hypothalamus exerts an important control over the anterior as well as the posterior lobe of the hypophysis. The evidence showing that the hypothalamus influences the gonadotropic functions of the hypophysis has been reviewed by Brooks (1940).

Clinical neurologists recognize adiposogenital dystrophy as a sign of damage to the hypothalamus; but for obvious reasons it has not been possible to study this condition experimentally in man. The syndrome has been produced in dogs by injuring this part of the brain (Bailey and Bremer, 1921; Biggart and Alexander, 1939). Various types of genital

*Aided by a grant from the Committee for Research in Problems of Sex, National Research Council.

dystrophy, unassociated with adiposity, can be produced in female guinea pigs by small hypothalamic lesions, reaching the ventral surface of the brain at the level of and just behind the optic chiasma (Dey, Fisher, Berry and Ranson, 1940; Dey, 1941). Some of these guinea pigs have atrophic ovaries and genitalia; others have hypertrophic genitalia and ovaries containing many well-developed follicles but no corpora lutea, showing that ovulation has not occurred; still others have normal ovaries and genitalia, run regular cycles and ovulate, but will nearly always refuse to accept the male. Occasionally one of these animals will mate and become pregnant. Most of the animals which do become pregnant fail to deliver in a normal manner.

In the clinical literature one finds hints that sterility in apparently normal women, abortions occurring without obvious cause, dystocia due to uterine inertia, and the convulsions of true eclampsia may be caused by a disturbance in function and balance of the endocrine glands. As a result of observations made on female guinea pigs with lesions in the hypothalamus, a method has been found for attacking such problems experimentally.

METHOD

Electrolytic lesions were placed in the hypothalamus of each of 74 female guinea pigs by means of the Horsley-Clarke apparatus as described in previous publications (Dey, Fisher, Berry and Ranson, 1940; Dey, 1941). The lesions reached the ventral surface of the brain between the optic chiasma and the mammillary body. Virgins weighing 400 to 500 Gm. were used. They were divided into 2 groups. One group, 40 in number, was placed with males and the lesions were made either immediately after pregnancy was established or else at a later stage of pregnancy. A second group of 34 females had the lesions placed before they were mated.

The majority of the animals that were operated upon while pregnant soon aborted or else resorbed their fetuses. Twelve of the animals died. After termination of pregnancy by abortion, resorption or delivery, the 28 remaining animals were again placed with males and treated in exactly the same manner as the 34 which were operated upon while still virgin.

The operated animals were now divided into groups of 6 and a male was placed with each group. At frequent intervals the males were either rotated or else replaced by fresh males. The females were observed daily for signs of pregnancy. When it was definitely established that a female was pregnant, it was separated from the male.

Daily observations were made on the pregnant animals and the condition of the vaginal membranes recorded. Toward the end of pregnancy they were observed at more frequent intervals. At the first signs of parturition they were placed under continuous observation until the delivery had terminated.

At frequent intervals during the course of the experiment, the animals were placed in individual cages and the water intake was recorded. The animals were then classified according to the quantity of water that they consumed. Those that drank from 50 to 90 c.c. of water daily were considered as having a mild polydipsia; 90 to 150 c.c., a moderate polydipsia; and over 150 c.c., a severe polydipsia. The degree of polydipsia gave some indication of the extent of atrophy of the posterior lobe of the hypophysis. The atrophic lobe is deficient in both the antidiuretic and the oxytocic principles (Fisher, Ingram and Ranson, 1936; Fisher, Magoun and Ranson, 1938).

At the end of the experiment the animals were autopsied and the brains, hypophyses, and ovaries prepared for histologic study.

RESULTS

Animals Which Became Pregnant Before Lesions Were Placed in the Hypothalamus.—Of the 40 animals in which the hypothalamic lesions were placed during pregnancy, 28 aborted or resorbed their fetuses and 12 retained pregnancy to term. The cause of the abortions has not been determined. Nineteen of the animals maintained pregnancy for four days or more and 11 of these for at least a week after the lesion had been made in the hypothalamus. This suggested that factors other than those arising as a direct result of the operation were responsible for the termination of pregnancy. To confirm this, two pregnant females were subjected to control operations which were similar in every detail to those performed upon the 40 animals of this group, except that electrodes were not inserted into the brain and no lesions were made. Both animals maintained pregnancy until term and delivered normally. Moreover, lesions were placed in the mammillary bodies of 2 other pregnant animals. These also maintained pregnancy until term.

The 12 operated animals that maintained pregnancy until term showed considerable variation in their ability to deliver. Three of them delivered normally after gestation periods which were of normal length. Two of these had a normal water intake while the third had a mild polydipsia. Five others were able to effect delivery after normal periods of gestation, although the mechanisms of parturition appear not to have been normal. Either the fetuses were born dead or else the mothers died a short time after the delivery of dead fetuses. Three of these animals had a mild polydipsia, one had a moderate polydipsia, and the fifth had a normal water intake.

Only 4 of the 12 animals showed disturbances of parturition as severe as those observed in cats with diabetes insipidus by Fisher, Magoun and Ranson (1938). One animal, which had a mild polydipsia, began to make bearing-down movements late in pregnancy. After these movements had continued for some time the animal went into a coma and died. At autopsy a mature fetus was found in utero. A second animal followed a course similar to that of the animal just described. When delivery was not effected after several days, however, the animal was killed and 2 mummified fetuses were found in utero. The animal had a mild polydipsia. The 2 remaining animals both effected delivery but not in a normal manner and several days late. One animal delivered a dead fetus on the seventy-third day of gestation and five days later delivered another dead fetus. The second animal delivered 1 dead and 2 mummified fetuses on the seventy-second day of gestation and four days later delivered another dead fetus. The first animal had a moderate polydipsia while the latter had a mild polydipsia. In contrast with these observations, Boling and co-workers (1939) have reported that the interval between the delivery of the first and last members of a litter of normal guinea pigs was less than thirty minutes in 79 out of 80 cases. The normal gestation period in the guinea pig varies in length between sixty-two and sixty-eight days.

Animals Which Became Pregnant After Lesions Were Placed in the Hypothalamus.—The 28 females, which survived the termination of pregnancy by resorption, abortion, or parturition, and the 34 that were operated upon while virgin, were placed with males. Only 13 of this entire group of 62 animals became pregnant, although they were kept with males for many weeks. The cause of this sterility has been discussed in other papers (Dey, Fisher, Berry and Ranson, 1940; Brookhart, Dey and Ranson, 1940, 1941; Dey, 1941).

Three of the 13 animals that did become pregnant delivered successfully after a gestation period of normal length. Two of these had a moderate polydipsia while the third had a severe polydipsia. One other delivered fetuses at term but both the mother and offspring died within two days after the delivery. The remaining 9 animals died either at term or shortly before term without delivering. Six of the animals died from disturbances which we shall refer to as convulsions. Two other animals died when not under observation, but from the condition of their bodies and of the cages, it is not unreasonable to assume that they died from similar convulsions.

These convulsions came on suddenly during the latter part of the gestation period. They occurred periodically and were characterized by weakness of the animal, generalized contractions of the skeletal muscles, running movements, gnashing of teeth, squealing and, finally, general prostration and death of the animal. Between seizures the extremities were quite spastic and muscular twitchings frequently occurred. The seizures varied in duration; and the frequency of their occurrence increased from the time of onset up until the time of the animal's death some three to twelve hours later.

The nature of these convulsions can be understood better by studying the protocol of one of the animals. This animal had a moderate polydipsia. It became pregnant and carried pregnancy until the forty-ninth day of gestation. On this day the animal appeared to be in good health during the routine morning examination. Five hours later, however, it was found lying on its side and it was undergoing vigorous convulsions. The vaginal membrane was closed and there were marked fetal movements. The convulsions when first observed occurred at intervals of approximately fifteen minutes. During the convulsions the animal would squeal and either gnash its teeth or else bite the wire netting of the cage. This activity resulted in severe lacerations of the gums and tongue and loosening of the teeth. The strong contractions of the abdominal muscles, the squealing and the apparent agony of the animal gave one the impression that the animal was bearing down in an attempt to expel the fetuses. The convulsions occurred more and more frequently until, some eight hours later, the interval between seizures was only about thirty seconds. At this time the respiration was slow and the temperature of the animal had fallen to 94.7° F. The animal died about nine hours after the onset of the disturbance. Marked fetal movements continued up until within several minutes of the animal's death.

The convulsions in this animal were similar to those in others of this group. It is interesting to note that at least 6 animals underwent con-

vulsions and died three days or more before parturition should have taken place. In a few animals the vaginal membranes opened and a bloody mucous discharge was extruded; in the others, the membranes remained closed throughout the entire procedure.

The fetuses appeared to be hyperactive, especially between successive convulsions. Their movements could both be seen and felt through the abdominal wall. These movements indicated that the fetuses were alive within a few hours of the death of the mother.

In spite of the vigorous activity of the animals during the convulsions, their temperatures fell to very low levels, in some cases so low that they could not be registered upon a rectal thermometer, i.e., to a point below 92° F. In order to determine if this fall in temperature preceded the convulsions, daily temperature readings were taken in one animal, the last of the series. At 9 A.M. on the day of death the rectal temperature of the animal was 102.3° F. which is within normal range for the guinea pig. The animal at that time appeared to be in good health; but at 5 P.M. it was found in convulsions. The temperature at this time was 97.8° F. From this observation, it is not possible to say whether the fall in temperature preceded the convulsions, but if so, the interval must have been very short. The observation serves to emphasize that the convulsions make their appearance suddenly in an apparently normal animal.

All except one of the animals that died of these convulsions had had diabetes insipidus as evidenced by a water intake that was considerably higher than that of the normal animal. This is of interest as indicating an atrophy of the posterior lobe of the hypophysis (Fisher, Ingram and Ranson, 1938).

At autopsy an incision was usually made in the abdominal wall and the uterus and the fetuses were lifted out. In several animals, however, the uterus and vagina were removed in toto. In each of these specimens it was found that the heads of 2 fetuses, one in either horn, were jammed tightly into the vaginal canal.

No differences could be detected between the ovaries of the animals of this group and those of normal animals which were killed on a corresponding day of pregnancy.

The hypothalami of the entire series of animals have been studied and described in a previous publication (Dey, 1941). The lesions in the animals which failed to become pregnant were bilateral, situated between the optic chiasma and the pre-mammillary nuclei, and they extended quite deeply into the hypothalamus. Those in the animals which became pregnant were similarly located but with the exception of 2 animals, they were either unilateral or else very superficially placed.

ADDITIONAL EXPERIMENTS

Since the work described in the preceding sections was completed we have had the opportunity to observe the effects of hypothalamic lesions on pregnancy and labor in 17 additional animals. All were young adults and the lesions were similar to those in the preceding experiments. Fifteen of the guinea pigs were pregnant when they

arrived in the laboratory and were operated upon soon after their arrival. Eleven of these promptly aborted. Three of the 4 remaining animals maintained pregnancy until term and delivered normally. Each had a normal water intake. The fourth animal, which had a moderate polydipsia, attempted to deliver thirty days after the lesion had been placed in the hypothalamus. When the animal was first observed in labor, a partially delivered fetus was hanging from the vagina. The animal failed to complete the delivery during the following hour so the investigator removed the fetus by traction. Three days later, the animal was again observed bearing down. After seven hours of these movements the head of a second fetus was exposed. One-tenth grain of dried posterior pituitary in saline was injected intraperitoneally. The bearing-down movements increased in frequency and twenty-five minutes later the delivery was completed.

One of the animals that had delivered normally became pregnant again. It delivered 2 dead fetuses on the seventy-seventh day of pregnancy, and a third dead fetus the following afternoon.

Only 2 of the animals that aborted following the operation became pregnant again. One animal, which had a severe polydipsia, was observed making bearing-down movements on the seventy-eighth day of pregnancy. Three hours later the head of a fetus was exposed. Delivery was not completed one and one-half hours later so the fetus was removed by the investigator. The second animal, which had a mild polydipsia, delivered 2 fetuses normally.

Observations were also made on 2 guinea pigs which were operated upon as virgins and later became pregnant. These were the only ones to become pregnant out of 14 virgin females which received the lesions and were later kept for several months with males. One of these 2 delivered 1 dead fetus on the seventy-fourth day of pregnancy. The other died on the sixty-seventh day of pregnancy. Two mature fetuses were found in the uterus. The first animal had a mild polydipsia while the latter had a normal water intake.

DISCUSSION

We believe that the abortions which follow the placing of lesions in the hypothalamus of pregnant guinea pigs are caused by the damage to this part of the brain since control operations, similar in every respect except that the electrodes were not inserted into the brain or were inserted into the mammillary bodies did not cause abortion. But the chief interest lies in the abnormalities seen in the animals which retained their fetuses. If we count those animals twice which were observed during 2 pregnancies, there were 16 which were pregnant before the lesions were placed and 18 which became pregnant after the operation. Out of the 16, pregnant before the lesion, 6 delivered normally, 5 died during delivery or delivered dead fetuses, and 5 had prolonged and difficult labors. Out of the 18 which became pregnant after the lesions had been placed, 4 delivered normally, 1 died following delivery, 4 died at or shortly before delivery (convulsions?), 3 had prolonged and difficult labors, and 6 died in convulsions shortly before term.

It should be noted that none of the animals which were pregnant when the lesions were placed developed convulsions, while at least 6 and probably 2 or 3 others which became pregnant after the operation died in convulsions which appeared suddenly late in pregnancy and were rapidly fatal. It is interesting to speculate on the relation of these convulsions to eclampsia. Although no satisfactory explanation can be given for the occurrence of these convulsions, it is possible that they may have resulted from a disturbed endocrine balance resulting from an alteration in pituitary hormones brought about by the hypothalamic lesion.

In a majority of the animals which went to term, there was obviously a serious disturbance in the mechanism of labor. Difficult and prolonged labor was observed in 7. Seven others which were not under such close observation died as a result of labor or delivered only dead fetuses. It is possible that in these also labor was unduly prolonged. In 6 of these 14 animals the onset of labor was definitely delayed, beginning on the seventy-second, seventy-third, seventy-fourth, seventy-seventh, seventy-eighth, and seventy-eighth days, respectively. As has already been stated, the normal gestation period for the guinea pig is sixty-two to sixty-eight days.

It is possible that the disturbances in parturition were due to a deficiency of the oxytocic hormone formed by the posterior lobe. Most of the lesions in the hypothalamus were so placed as to interrupt at least a part of the fibers of the supraopticohypophysial tract. It has been shown that when this tract is completely interrupted by hypothalamic lesions in cats the posterior lobe of the hypophysis undergoes atrophy, and its content of the antidiuretic, pressor, and oxytocic hormones is decreased almost to the vanishing point (Fisher, Ingram and Ranson, 1938). As a result of the loss of antidiuretic hormone, diabetes insipidus occurs. In this way diabetes insipidus was produced in 85 cats. This number included 7 that had had lesions placed in the hypothalamus during pregnancy. These 7 went to term, but had prolonged labors and all but one of them died. It was suggested that the dystocia might be due to deficiency of the oxytocic hormone, and the literature bearing on the significance of this hormone for labor was reviewed (Fisher, Magoun, and Ranson, 1938).

Whatever may have been the cause of the dystocia in these cats it is interesting that slightly less than ⅓ of the pregnant guinea pigs with similar hypothalamic lesions delivered normally. About half of them had definitely prolonged or delayed labor or delivered dead fetuses. These animals would seem to have had a disturbance essentially similar to that in the cat. The 6 guinea pigs that died in convulsions presented an entirely different clinical picture, but it is possible that the cause of the convulsions may have been in some way related to the cause of the dystocia in the other animals.

In the guinea pigs water exchange was measured only by the water consumed and the observations on diabetes insipidus were, therefore, less accurate than on the cat where both fluid intake and output were carefully measured. The majority of the guinea pigs which had prolonged or delayed labor or delivered dead fetuses had shown an in-

creased water intake but a few had shown a normal intake. On the other hand about half of those which delivered normally had shown increased water intake. It is, of course, possible that the oxytocic hormone might have been reduced below its effective level while the antidiuretic hormone was still present in adequate amounts . . . but these experiments on the guinea pig can certainly not be offered as convincing evidence that the oxytocic hormone plays an essential part in labor.

The animals which became pregnant after lesions had been placed in the hypothalamus belonged to the group which ran regular sex-cycles following the operation and which must, therefore, have had a fairly normal secretion of pituitary gonadotropic and ovarian hormones. The hypophyses were not directly involved in the lesions. The ovaries were histologically normal. But, since many of the other guinea pigs with hypothalamic lesions showed clear evidence of abnormalities in ovarian and pituitary gonadotropic function, it is possible that those which became pregnant also had similar abnormalities of a degree insufficient to prevent breeding. The polydipsia shown by most of the animals is evidence that the antidiuretic hormone of the posterior lobe of the hypophysis was deficient in amount and this would indicate a probable deficit in oxytocin (Fisher, Ingram and Ranson, 1938). It is, therefore, difficult to avoid the suspicion that abnormalities in pituitary and ovarian hormones may have been responsible for the disturbances in pregnancy and labor described in this paper.

SUMMARY

Female guinea pigs with medially placed lesions in the hypothalamus, reaching the ventral surface of the brain at the level of and just behind the optic chiasma were usually sterile, although some did become pregnant. These usually had unilateral or very superficial lesions.

Slightly less than one-third of the pregnant guinea pigs with hypothalamic lesions delivered normally. About half of them had definitely prolonged or delayed labor or delivered dead fetuses. It was not possible to establish definitely a relationship between this dystocia and a deficit in oxytocic hormone, but it may be that such a relationship exists.

Six of the pregnant guinea pigs with hypothalamic lesions died in convulsions which appeared suddenly late in pregnancy and were rapidly fatal. These convulsions are of interest because of their resemblance to eclampsia.

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THE INTRAVENOUS ADMINISTRATION OF PARALDEHYDE DURING LABOR

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THE use of intravenous paraldehyde for obstetric analgesia and anesthesia has not, to our knowledge, been previously reported. With the purpose of determining the suitability of this method of administration this study was undertaken. We present our observations upon 100 patients who received intravenous paraldehyde during the course of labor.

Since the introduction of paraldehyde as an obstetric analgesic by Rosenfield and Davidoff[1] in 1932, the popularity of this drug has steadily increased. Its comparative safety for both mother and child is becoming more widely recognized. Though paraldehyde is usually administered by the rectal or oral route, parenteral use has been advocated from time to time for various purposes. Johnson[2] has administered paraldehyde parenterally for the control of pain and convulsive states. One of his patients received 60 c.c. of paraldehyde by intramuscular injection over a period of twenty-four hours with no harmful effects. The disadvantage of the intramuscular route is that severe burning and local irritation immediately result, though Johnson observed no cases of muscle necrosis. Intravenous paraldehyde was first used by Noel and Souttar[3] in 1912 as a hypnotic, analgesic, and anesthetic agent. Robinson[4] recommended intravenous paraldehyde for the production of narcosis in the performance of pneumoencephalography. His maximum single dose was approximately 0.4 c.c. per kilogram of body weight. Basing his work on animal experimentation, Beauchemin and others[5] calculated the lethal dose for a 150-pound man to be 40 to 60 c.c. if the paraldehyde was given intravenously. Caldwell[6] used comparatively small doses of intravenous paraldehyde (1 to 3 c.c.) to control satisfactorily the convulsions of eclampsia. Paraldehyde is commonly stated to be the least toxic of the hypnotic drugs.[7]

PREPARATION AND ADMINISTRATION

For intravenous use an aqueous solution of paraldehyde is much to be preferred to the undiluted drug, since the latter causes spasms of coughing. The assumption that this reaction may result from lung irritation produced by small emboli of undissolved paraldehyde, is suggested by the fact that paraldehyde is rather slowly soluble. At any rate we know that this reaction may be eliminated entirely by dissolving the paraldehyde in water. Paraldehyde is soluble to the extent of one part paraldehyde to nine parts of water at room temperature. One hundred cubic centimeters of the 10 per cent solution, made by adding 10 c.c. of paraldehyde to 90 c.c. of sterile distilled water, usually suffices. Fresh solutions were prepared shortly before the time of intravenous administration, using paraldehyde of the same U.S.P. quality as is used for oral and rectal administration. Since comparatively large volumes of the aqueous solution are required, it is necessary to use a 50 c.c.

Luer syringe. The solution was injected into the antecubital vein. The rate of injection was governed by the individual response and according to the type of response desired. The usual injection time for 50 c.c. of the aqueous solution was two to three minutes. Caution should always be practiced, but seldom is there indication to alter the injection rate when the dose is only 1 c.c. of a 10 per cent solution per kilo of body weight.

In order to be able to make a more accurate evaluation of the effects of intravenous paraldehyde, no other drug was administered during the course of labor. An ether anesthetic was usually given at the time of delivery unless intravenous paraldehyde was being given as the general anesthetic.

Of the 100 patients, one group received a single intravenous injection of paraldehyde from ten minutes to nine hours before the time of delivery, and it is from this group that several blood paraldehyde curves were determined. The second and largest group received intravenous paraldehyde from three to thirty minutes prior to the administration of a rectal dose of paraldehyde. In the third group of patients, an attempt was made to use intravenous paraldehyde as a general anesthetic at the time of delivery.

BLOOD LEVELS FOLLOWING THE USE OF INTRAVENOUS PARALDEHYDE

According to Gardner and others,[8] it is usually necessary to produce a blood paraldehyde level of 15 to 20 mg. per 100 c.c. if amnesia is to be expected. After observing that most patients who received 1 c.c. of 10 per cent paraldehyde solution per kilogram of body weight experienced a period of complete amnesia, it was decided to determine the blood paraldehyde levels following the administration of this dose. The analytical method as described by Levine and Bodansky[9] was used. Blood samples were taken at 5-, 15-, 30-, 60-, and 120-minute periods. Referring to Fig. 1, one sees that the 5 curves are similar in each instance, and for this reason, further determinations were not thought to be indicated. The highest maximum blood level for the five individual curves was 22 mg. per 100 c.c., and the lowest maximum level for the group was 14.8 mg. per 100 c.c. One of this group of five patients failed to experience a definite period of complete amnesia. This patient's maximum blood paraldehyde concentration was 19.4 mg. per 100 c.c.

ANALYSIS OF RESULTS

Twenty-nine patients who received neither previous nor subsequent medication of any kind were given a single intravenous injection of paraldehyde from ten minutes to nine hours before delivery. In 23 of this group, delivery occurred within one hour and a half of the time of administration. Of this group of 29 patients, 17 received 0.7 c.c. of 10 per cent paraldehyde per kilo of body weight, and 12 received 1 c.c. of 10 per cent paraldehyde per kilo, the actual amount of 10 per cent solution varying from 36 to 79 c.c. Of the 17 patients who received 0.7 c.c. of 10 per cent paraldehyde per kilo of body weight, 8 experienced a period of complete amnesia, while the other 9 had fair to complete analgesia for a period of

from thirty to sixty minutes. Of the 12 patients who received 1 c.c. of 10 per cent paraldehyde per kilo, 10 experienced a period of complete amnesia for twenty to ninety minutes, while the other 2 patients had good analgesia. The majority of these 29 patients were multiparas in whom delivery was imminent, and it is likely that it is under these circumstances that intravenous paraldehyde will find its greatest field of usefulness. The screaming multipara who is reaching the end of her toil can be rapidly and effectively calmed with intravenous paraldehyde.

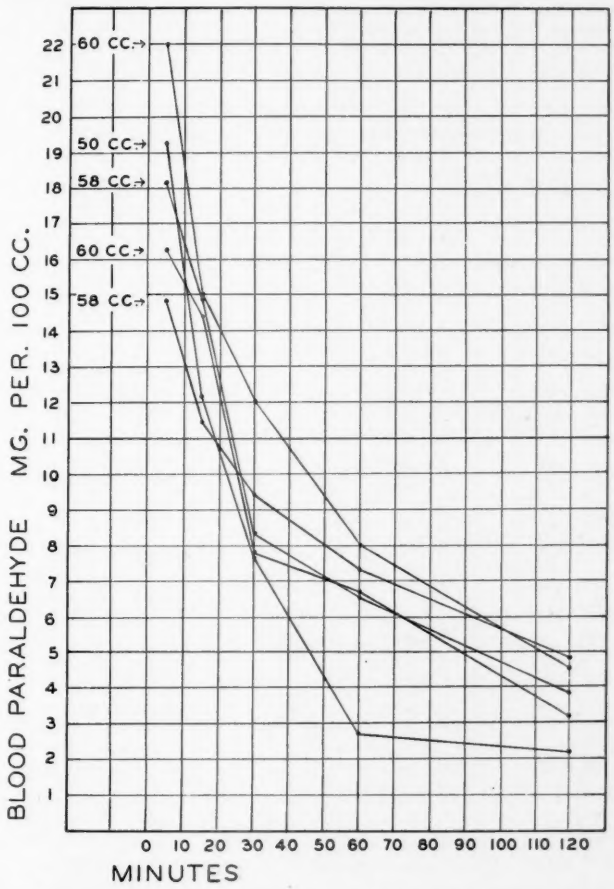

Fig. 1.—Blood paraldehyde concentrations following intravenous administration of 1 c.c. of 10 per cent solution per kilogram body weight. Figures at top of each curve represent the dose administered in cubic centimeters of 10 per cent aqueous solution.

The second and largest group consisted of 58 patients who received intravenous paraldehyde in conjunction with rectal paraldehyde in olive oil. Of these, 25 received 0.7 c.c. of 10 per cent aqueous solution per kilo of body weight and 33 received 1 c.c. of 10 per cent solution per kilo, the actual dose varying from 40 to 82 c.c. The rectal dose was 0.4 c.c. of undiluted paraldehyde per kilo, the actual amount varying from 20 to 36 c.c. The interval elapsing between the intravenous and rectal dose varied from three to thirty minutes, all but 4 patients receiving the rectal paraldehyde within twenty minutes after the intravenous paraldehyde. Of these 58 patients, 14 remembered the administration of the rectal paraldehyde, and most of these 14 patients had received the smaller intravenous dose of 0.7 c.c. of 10 per cent solution per kilo administered more than ten minutes before the rectal dose was given. In the group of 33 patients who received intravenously 1 c.c. of 10

per cent paraldehyde solution per kilo of body weight, only three remembered getting the rectal dose. It was hoped that the intravenous paraldehyde would aid the patient in retaining the rectal dose, but we found that approximately 40 per cent of the patients expelled all or part of it. Of the 35 patients who retained all of the rectal medication, 31 experienced complete amnesia for the remaining course of labor, while the other 4 experienced partial amnesia and marked analgesia. The average duration of labor for these 58 patients, most of whom were primiparas, after the intravenous paraldehyde injection, was four hours and fifty-three minutes. We found that by the use of this combination of intravenous and rectal paraldehyde, amnesia and analgesia may be produced from the moment the intravenous paraldehyde is injected.

The third group of 14 patients were given intravenous paraldehyde at the time of delivery as a general anesthetic (Table I). Patient 1, a para i, had a funnel

TABLE I. PERTINENT DATA OF 14 PATIENTS RECEIVING INTRAVENOUS PARALDEHYDE DURING DELIVERY

PATIENT	DOSE C.C. OF 10% AQUEOUS PARALDEHYDE	DOSAGE C.C./KILO	DURATION OF ANESTHESIA BEFORE DELIVERY MINUTES	AMNESIA	ANALGESIA
1	125	0.260	30	Complete	Complete
2	71	0.100	20	Complete	Complete
3	80	0.114	15	Complete	Complete
4	84	0.100	20	Complete	Complete
5	100	0.133	20	Complete	Complete
6	50	0.070	5	Complete	Complete
7	150	0.200	20 minutes and during repair of episiotomy	Complete	Complete
8	90	0.136	25	Complete for pain	Complete
9	100	0.142	15	Complete	Complete
10	94	0.140	15	Partial	Marked
11	46	0.070	12	Partial	Marked
12	100	0.146	20	None	Marked
13	58	0.070	8	None	Marked
14	50	0.070	15	None	Marked

pelvis and was delivered by low forceps. Patient 2 had a temperature of 103.2° F. at the time of delivery, and eight hours before delivery the fetus had died in utero. Patient 6, was a severe pre-eclamptic who delivered a macerated fetus; in addition to her intravenous paraldehyde she had received 14 c.c. of paraldehyde per rectum eight hours before delivery. Patient 7, a primipara, had received 7.1 c.c. of the intravenous paraldehyde and 30 c.c. of paraldehyde per rectum six hours before delivery. At the time of delivery this patient received an additional intravenous injection of 15 c.c. of the 10 per cent aqueous paraldehyde solution while forceps were being applied and the episiotomy repaired. This patient was never sufficiently controlled to repair the episiotomy satisfactorily, although she showed signs of deep anesthesia, as evidenced by tongue swallowing and loss of pharyngeal and corneal reflexes. Patient 8, a primipara, was delivered by low forceps and episiotomy, the episiotomy site being injected with novocaine. Patients 3, 4, 5, 9, 10, 11, 12, 13, and 14 were all normal multiparas who delivered spontaneously. Of the entire group of 14 patients, 9 experienced complete amnesia for pain, while 7 had amnesia for all events. All patients agreed that the pain was lessened.

Reactions.—In this group of 100 patients we failed to observe any untoward reactions to the intravenous paraldehyde. In 44 per cent of the patients more or less arm pain was produced during the time of injection. The pain characteristically follows the course of the veins. Some patients felt pain as high as the subclavian veins. This arm pain may be practically eliminated by elevating the arm during the

course of injection. Six per cent of the patients developed a mild hiccough which lasted only a few minutes. Vomiting occurred in 3 per cent of the patients within a few minutes after intravenous paraldehyde. As all of these patients were in active labor, the vomiting could not be definitely attributed to the paraldehyde. Mild coughing seizures, probably due to incomplete solution of the paraldehyde in water, occurred immediately in two of the patients.

Pulse.—The pulse was counted immediately before and after the intravenous injection of paraldehyde. Fifty-four per cent showed a rise in pulse rate of from 2 to 40 beats per minute. It is not uncommon to see the pulse rate jump 20 to 30 beats during the course of injection. Twenty-five per cent of the patients had a slowing of the pulse rate. The change in this direction is less marked, the fall usually not amounting to more than 10 beats per minute. Twenty-one per cent showed no change in pulse rate.

Blood Pressure.—Neither systolic nor diastolic pressures showed any alteration of consequence. Forty-eight per cent showed a rise, 32 per cent a fall, and 20 per cent showed no change.

Respirations.—With the usual dose of 1 c.c. of 10 per cent paraldehyde per kilo there is usually little or no change in the respiratory rate, but when much larger doses are administered a definite stimulative effect is seen. The rate may be accelerated to 30 or 40 per minute, and the depth increased as was observed in several patients who received relatively large doses. For example, one patient was given 15 c.c. of intravenous paraldehyde at the time of delivery after having had rectal paraldehyde previously. We interpreted this labored respiration as an indication of overdosage.

Patient's Conduct.—As with all forms of narcosis, the actions of the patient are unpredictable. Sleep between pains was invariably produced with the 1 c.c. of 10 per cent paraldehyde per kilo dose.

Effect Upon Fetus.—The rate of the fetal heart showed no significant change. Some degree of apnea was noted in 6 infants, but never to a dangerous degree. Two of these infants were showing signs of distress before delivery as indicated by the passage of meconium. The uncorrected fetal mortality was 4 per cent. Two macerated infants were born of toxemic mothers. One infant died eight hours before the administration of intravenous paraldehyde. The fourth infant was ten weeks premature and died in forty-eight hours from intracranial hemorrhage. Obviously the intravenous paraldehyde was in no way a causative factor in these fetal deaths.

Contraindications.—During this study no patients were encountered in whom it was thought that intravenous paraldehyde was contraindicated. Nine of the patients were considered pre-eclamptic, 1 had chronic nephritis, 2 had rheumatic heart disease, 1 had epilepsy, and 1 had a temperature of 103.2° F. from an unknown cause.

SUMMARY

1. One hundred patients were given intravenous paraldehyde during the course of labor. The dosage varied from 0.7 to 1 c.c. of 10 per cent solution per kilo of body weight, the actual amounts varying from 36 to 150 c.c. of 10 per cent paraldehyde for a single injection.

2. Twelve patients received 1 c.c. of 10 per cent paraldehyde per kilo during the course of active labor, and 10 of these experienced a period of complete amnesia of usually less than one hour. Seventeen patients received 0.7 c.c. of 10 per cent paraldehyde per kilo during the course of active labor, and, of these, 8 experienced a period of complete amnesia.

3. Fifty-eight patients received intravenous paraldehyde from three to thirty minutes before a rectal dose of paraldehyde. Of the 43 who

received 1 c.c. of 10 per cent paraldehyde per kilo, only 3 remembered receiving the rectal drug.

4. Intravenous paraldehyde was used as an anesthetic for delivery in 14 patients. The minimum dose was 0.7 c.c. of 10 per cent paraldehyde and the maximum dose was 2.6 c.c. of 10 per cent paraldehyde per kilo. Only the larger doses of 1 to 2 c.c. of 10 per cent paraldehyde per kilo may be expected to produce complete analgesia and amnesia during the second stage of labor.

5. In no instance was a serious reaction encountered. Arm pain was experienced by 44 per cent of the patients during the course of injection. A mild coughing seizure occurred in 2 per cent and hiccoughs in 6 per cent.

6. Respiration and blood pressure are not essentially altered with the usual dose of 1 c.c. of 10 per cent paraldehyde per kilo, but with much larger doses, labored respiration may be encountered. The pulse rate was accelerated in 54 per cent, it not being uncommon to see an immediate increase of 20 to 30 beats per minute.

7. There is no evidence that intravenous paraldehyde produces any effect upon the infant.

8. The highest maximum concentration of blood paraldehyde as seen in 5 patients who received 1 c.c. of 10 per cent solution per kilo was 22 mg. per 100 c.c.

9. The beginning effect of intravenous paraldehyde is noted in ten to twenty seconds after the injection is started.

CONCLUSIONS

Paraldehyde, in 10 per cent solution, dosage as outlined above, may be safely employed intravenously during labor without deleterious effect upon infant or mother.

Whereas, we do not recommend routine intravenous administration of paraldehyde during labor, we do feel that this method has a definite field of usefulness, under circumstances in which rapidly effective analgesia, of brief duration, is indicated.

The blood analyses in this study were done in the Maternal and Child Health Laboratories under the direction of Dr. V. M. Wilder.

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THE SHORTENING OF LABOR WITH SYNTROPAN*

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THE duration of labor,[1] usually conceded to be about eighteen hours in the primipara and about twelve hours in the multipara, has ever been an important consideration in obstetrics, in that many of the difficulties arising during and after delivery have their origin directly or indirectly in long labor. A material and harmless shortening of the parturition process, particularly the first stage, seemingly should result in the elimination of certain frequently encountered obstetric complications. Some of the complications which might be obviated include: uterine inertia; infection; deleterious effect on mother, particularly in the presence of cardiac disease, renal damage, or pulmonary tuberculosis; and finally a deleterious effect on the child.

These are but a few of the many dangers associated with prolonged labor. If we consider as well that the patient would be spared much of the pain and other incidental discomforts, all the advantages of harmlessly shortening the parturition process become obvious.

It is not surprising that numerous obstetricians have interested themselves in the problem of shortening the duration of labor and that various methods of doing so have been advocated. Certain of these may be mentioned, only to be condemned.[2, 3]

The undesirability of long-continued administration of the usual obstetric analgesics is well recognized. One of the pitfalls from overenthusiasm in this direction, and one which certainly should be avoided, is depression or abolition of the so-called protective reflexes, as for example the pharyngeal reflex. Interference with this particular mechanism, alone, may have grave consequences.

An inquiry into the etiology of prolonged labor or dystocia will serve very well in introducing the treatment which is the subject of this report. The causes of dystocia are many, and are commonly classified as fetal and maternal. Further remarks on the former type, i.e., that which is due to the shape, size, and position of the fetus is not germane to this discussion. Neither are we directly concerned with pelvic dystocia or with difficult labor brought about by a disproportion between the size of the baby and the dimensions of the birth canal. As common, if not more so than the varieties already mentioned, is the condition known as cervical dystocia, which may be a manifestation of any one of several types of abnormal mechanisms, or a combination of abnormal mechanism plus other factors. There is, for instance, that common abnormality where incarceration of the anterior lip of the cervix delays or prevents descent of the presenting part. Such a condition from the very nature of the mechanics involved, requires correc-

*Read at a meeting of the Chicago Gynecological Society, March 21, 1941.

tion by manipulative means. On the other hand, the fact that a functional disturbance of the cervix, such as cervical spasm, may be a cause of dystocia, has been recognized by many workers[4-7] and recently commented upon by de Oliveria Sarmento.[8]

In a search for a preparation which would minimize the risk of childbirth by shortening labor, without introducing any new elements of danger, the nonnarcotic antispasmodic, syntropan* was selected for trial. This is the phosphate salt of the tropic acid ester of 3-diethyl-amino-2, 2-dimethyl propanol. The drug has been demonstrated to have a definite antispasmodic action on spastic smooth muscle, due jointly to inhibition of the parasympathetic innervation and to direct relaxing action on the muscle cell.[6-11] The antispasmodic action is similar to that of atropine, but is not attended by the latter's undesirable by-effects.[12, 13]

Although the exact mechanism of the effect of syntropan on labor must await further physiologic and pharmacologic experiment, its relaxing effect on the uterine cervix would seem to be the rationâle for its efficacy in hastening cervical dilatation, thus shortening the duration of labor. Syntropan has been used in obstetrics by several investigators.[5-7, 14]

The principle of antispasmodic treatment would seem to be removal of resistance offered by the spastic cervix, at the same time preventing increase in rhythmic contraction and tension in the uterus as a whole which would normally be engendered by cervical resistance. Ivy and Rudolph[15] have pointed out that the uterus during labor is subdivided anatomically and physiologically into upper and lower segments between which a distinct functional difference may be observed. Spasm of the lower uterine segment (including the cervix), sometimes referred to as a hyperkinetic cervix, may result from nervous influences such as fear and anxiety. The familiar "constriction ring dystocia" may also occur, and is a condition which logically could be expected to respond to an antispasmodic drug.

METHOD

Our procedure consisted of the oral administration of two tablets of syntropan, 50 mg. each, to an experimental group of 34 patients when cervical dilatation of several centimeters was first noted. No other medication of any kind was given. This series of patients included both primiparas and multiparas. The progress of labor was closely observed in the experimental group and in a comparable number of untreated cases constituting the control group. Patients in both groups were taken at random and not selected according to their obstetric histories. The results, i.e., effect upon duration of labor, are given in tabular form (Tables I and II). There was a dramatic reduction of labor-time in the syntropan-treated cases.

TABLE I. PATIENTS TREATED WITH SYNTROPAN

	NUMBER OF PATIENTS	FIRST STAGE	AVERAGE DURATION OF LABOR		TOTAL	AVERAGE WEIGHT OF INFANT AT BIRTH IN POUNDS
			SECOND STAGE	THIRD STAGE		
Primiparas	14	5 hr. 20 min.	23 min.	10 min.	5 hr. 53 min.	7½
Multiparas	20	5 hr. 20 min.	25 min.	11 min.	5 hr. 56 min.	8½

*Supplied by Hoffmann-La Roche, Inc., Nutley, New Jersey.

TABLE II. CONTROL PATIENTS

	NUMBER OF PATIENTS	FIRST STAGE	AVERAGE DURATION OF LABOR		TOTAL	AVERAGE WEIGHT OF INFANT AT BIRTH IN POUNDS
			SECOND STAGE	THIRD STAGE		
Primiparas	9	19 hr. 10 min.	3 hr. 35 min.	12 min.	22 hr. 57 min.	7
Multiparas	17	15 hr.	2 hr. 50 min.	11 min.	18 hr. 1 min.	8⅓

With the warranty of the encouraging results obtained in this small but convincing series of cases, the use of syntropan in the same manner was observed in a very much larger series of cases. The results in this larger series are recorded in Table III. The same dramatic reduction in labor-time was obtained, the first stage of labor averaging six hours and twenty-one minutes in 60 multiparous patients and nine hours and nine minutes in 42 primiparous patients.

TABLE III. PATIENTS TREATED WITH SYNTROPAN

	NUMBER OF PATIENTS	FIRST STAGE	AVERAGE DURATION OF LABOR		TOTAL	AVERAGE WEIGHT OF INFANT AT BIRTH IN POUNDS
			SECOND STAGE	THIRD STAGE		
Primiparas	42	9 hr. 9 min.	1 hr. 2 min.	7 min.	10 hr. 18 min.	7¼
Multiparas	60	6 hr. 21 min.	29 min.	5 min.	6 hr. 45 min.	7⅔

COMMENT

Upon comparing the labor-times of the control patients with those of treated patients, it can be seen that labor in the treated cases was, on an average, about one-half as long as in the control cases. Even in three cases in which version and extraction were done, the first stage of labor was definitely decreased in time.

In none of the treated cases was the duration of the second stage of labor longer than in the average normal; to the contrary, it was decidedly shorter. Thus it appear that the antispasmodic, syntropan, unlike sedatives, does not decrease voluntary or involuntary expulsive efforts. Averages for duration of the third stage are admittedly not important and are included only for the sake of completeness.

Cesarean section was performed in four of the total series of cases because of dystocia. While the findings in such abnormal cases markedly elevate the averages in the statistics for the entire series of cases, they have been included because each and every maternity case seen by us, while the investigation was in progress, received syntropan. In these cases the cervix dilated satisfactorily under the influence of syntropan, but the bony pelvis either did not permit delivery or a malposition existed, hence version, cesarean section, or forceps were employed.

The use of syntropan in labor apparently has no deleterious effect upon the infant. In the series of 102 cases (Table III), the condition of the infant immediately after delivery was "good" in 97 cases, "fair"

in 3 cases, "cyanotic" in 1 case, and "stillborn" in 1 case. The average birth weight of the infants in this series was seven and one-fourth pounds, well within the normal range, hence weight of the infant can be eliminated as a factor which might otherwise have abnormally influenced duration of labor in the series as a whole.

SUMMARY

1. The rationâle of the use of syntropan in labor is discussed.

2. The effect of the drug on labor-time in a series of 34 cases is demonstrated by comparison with the labor-time in a series of 26 untreated cases.

3. The effect of syntropan on the duration of labor in an additional group of 102 patients is also recorded.

4. The findings indicate that syntropan materially shortens labor.

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DISCUSSION

DR. DAVID S. HILLIS.—Various efforts to shorten labor have often been the source of injury to mothers and babies. As a rule the effort is made to shorten labor more for convenience than for any justifiable reason. On this account a discussion of this question is undertaken with some hesitation.

Some months ago, our attention was called to the work that Dr. Stoll has just reported, and we undertook to study the effect of syntropan on the duration of labor in Cook County Hospital. A report of the results of this study on 600 cases will be made in due time. It may be said now that no serious objections were found to this method. The average length of labor with syntropan was shorter than without syntropan. The number of prolonged labors among the syntropan cases was greater than among the controls. In short, our experiences correspond quite closely with that which Dr. Stoll reported this evening.

DR. H. C. HESSELTINE.—It would be a real contribution if we could do something that would dependably shorten labor and yet do so with safety for both the mother and the baby. Many promising methods have come and finally disappear, either by formal retraction in the literature or through general discard, because they either did not work out or the earlier observations have not been sufficiently well controlled.

Some time ago Adair and Dieckmann, while making a special metabolic study on gravid patients, found that the duration of labor in primiparas was fifteen hours, while their control cases had a labor of thirteen hours. This difference is within the experimental range. The multiparas likewise in both the treated and control series had appreciably shorter labor than the textbook averages. Thus, it is evident that the length of labor may need to be re-established for each individual study because of possible special local factors, such as type of patient, obstetric procedures, technique, etc.

Dr. Morton, our associate, is investigating syntropan for its effect upon uterine motility. The question may be raised: if syntropan relaxes the cervix, what happens to the uterus? There is a report in the literature that this preparation may arrest threatened abortion. If such is the case, what would cause the drug to act at one time in pregnancy upon the corpus uteri and another time upon the cervix uteri? Surely there is need for adequate pharmacologic and physiologic study before free and indiscriminate clinical use is justified.

If labor is shortened, it may result either from increasing uterine contractions or by lessening resistance to dilatation and expulsion. It may take a very large series to establish statistically that the labor is shortened, and a larger number still to show that a shortened labor is possible without increased risk to either the mother or baby.

SOME ETIOLOGIC FACTORS IN STERILITY*

A Study of 483 Patients Admitted to the Sterility Clinic, Bellevue Hospital

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IT IS not our intention in the present study to review the literature nor outline the therapy of sterility. There have been greater advances in the diagnosis and treatment of sterility since 1920 than in the previous centuries. Because of this fact those with involuntary sterility have taken heart. Childless couples now seek medical counsel with far more justifiable optimism than ever before. In the past, manual examination with surgical correction of existent anatomic abnormalities, if found, were the sole procedures the physician had to offer. The results of this operative era were notoriously poor. Prior to 1920, the wife was considered the principal cause of sterile unions except wherein the husband was grossly and obviously incapable of performing the sex act. It remained for a widely dispersed group of pioneer workers, Huhner, Rubin, Ogino, Knaus, Hartman and many others, to alter our concept of sterility. Indeed, the whole field of normal human reproduction has been profoundly changed and clarified by the work of these men. There is room for additional clarification. For example, we have as yet no laboratory method of proving the fertility of a given semen specimen. Although we believe that for all practical purposes, we can recognize a really fertile specimen, an occasional exception is reported. However, an absence of spermatozoa or the finding of very few or only dead sperm in properly collected and transported specimens on repeated occasions is presumptive evidence of male infertility. It is now universally recognized that no sterile woman should be subjected to serious operation until her husband's semen is known at least to contain living spermatozoa. Even this commonsense dictum has been in force for an incredibly short time. It is to be hoped that our

*Aided by a grant from the National Committee on Maternal Health, Inc.

knowledge of the factors influencing sterility will expand in the future as rapidly as it has in the past few years.

In the present study it is proposed to report on some of the etiologic factors found in a group of 483 patients who sought admittance to the Gynecological Clinic of Bellevue Hospital, solely because of their inability to have a child or an additional child.

When the clinic was assured that the patient desired a baby and not simply an improvement in her own health, which some fancied a pregnancy would bring, a detailed history was taken upon a special blank designed to record pertinent factors in the past life of both husband and wife. The woman was warned that the investigations might take months and that treatment might require even a longer period of time. The patient was informed that she must be prepared to come to the clinic at weekly intervals or as often as advised.

A complete and adequate pelvic examination, including measurement of the uterus, was then performed and recorded. The woman was instructed to return with a specimen of her husband's semen the following week.

A complete routine study was then initiated on those women whose mates seemed to offer reasonable hope of fertilization. This study included a medical history, a complete physical examination in selected cases, a Rubin test with hysterosalpingography in doubtful cases, basal metabolism test, Wassermann test and an urinalysis. Cases of obvious endocrine dysfunction were referred to our Endocrine Clinic for study. Endometrial biopsy, cervical smear for gonococcus, complete blood counts, blood chemistry, reference to the medical clinic for systemic investigation were ordered as indicated. The weight, the date and duration of her last menstrual period were recorded upon each clinic visit. Many of the patients failed to return for complete investigation and our follow-up upon these cases was necessarily sketchy due to the floating character of the clinic population and our lack of a special worker to trace them. Therefore, some of our records are incomplete both diagnostically and with respect to end results. Despite these drawbacks, however, we feel justified in reporting the incidence of etiologic factors so far as found.

Our patients were all married women of the lower economic and social strata. Their ages varied between 17 and 44 years. There were 26 under the age of 20 and 6 patients were over 40 years of age. Over half (276) were between the ages of 20 and 29. Two patients who had been married only two months, and in whom conception had not occurred, had become impatient and sought aid. These patients were examined and instructed to return later if conception failed to occur. Seven had been married fifteen years or more without a pregnancy. The longest duration of marriage was twenty-four years although this couple had had two children and two spontaneous abortions, the latest having taken place five and one-half years before admittance. Nearly half (239) were admitted to the Clinic following one to four years of married life. Eighty-three per cent (401) were admitted during the first nine years of marriage. There were 34 couples who had been married more than ten years with sterile unions and who still hoped

to have children. Primary sterility was diagnosed in 284 cases. One hundred and ninety-nine patients with secondary sterility gave a collective history of 384 pregnancies, 225 of which had terminated in abortions and 159 in viable births. Among the 199 cases of secondary sterility, 42 (21 per cent) had been previously married, while among the 284 patients who had never conceived only 15 (5 per cent) were now married for the second time. Of the 199 patients who had previously been pregnant, 135 (68 per cent) had experienced one or more abortions. Of this group, 13 could be termed habitual aborters, having had from 3 to 8 spontaneous abortions each.

In 43 cases (22 per cent), sterility was preceded by 1 to 4 induced abortions. Four patients each gave a history of one ectopic pregnancy. One of the latter conceived while under treatment, but nidation was again extrauterine and a laparotomy had to be performed.

Those contributing etiologic factors reported in the medical histories, which were thought possibly pertinent to the present sterility were listed in Table I.

TABLE I. CONTRIBUTING ETIOLOGIC FACTORS TO STERILITY (REPORTED IN HISTORY)

	TOTAL	%	PRIMARY STERILITY	%	SECONDARY STERILITY	%
Appendectomy	87	18.0	49	14.0	38	19.0
Mumps	51	11.0	32	11.0	19	10.0
Laparotomy (other than appendix)	47	10.0	20	7.0	27	14.0
Dilatation and curettage	26	5.0	8	3.0	18	9.0
Salpingitis	22	5.0	13	5.0	9	4.0
Leucorrhea	22	5.0	17	6.0	5	2.5
Sepsis (post-partum or postabortum)	15	3.0	--	--	15	8.0
Gonorrhea	14	3.0	9	3.0	5	2.0
Syphilis	8	2.0	4	1.4	4	2.0
Thyroidectomy	4	1.0	2	0.7	2	1.0
Difficult labor	2	0.5	--	--	2	1.0

There was little difference in the histories of the primary and secondary sterility except in those conditions which were directly dependent upon pregnancy and its termination. Laparotomy for appendicitis and other causes was found more frequently in the secondary sterility group while gonorrhea and its complications (salpingitis, hydrosalpinx, and leucorrhea) evidence a small but constant lead in the primary sterility group.

Our information concerning the male partner in these sterile marriages was sparse. The wives showed amazing ignorance of their husbands' pasts, and we had no facilities for interviewing the men themselves. The semen examination was our sole basis of evaluating the male fertility.

Some of those sterile males who appeared totally incompetent (azoospermia) were referred to urologists, chiefly Dr. Robert Hotchkiss, and some to Dr. Ira Kaplan for x-ray stimulation. Six husbands were known to have had gonorrhea, 1 syphilis, and 1 diabetes.

The frequency of coitus among 402 couples (83 per cent) was from one to four times a week. Among 46 couples who reported sexual intercourse more than four times a week, only 7 males had motile sperm. Of the 21 couples whose reported coital frequency was less than once a week only 6 had motile sperm.

The greatest frequency of coitus was 4 or 5 times daily, reported by a female dwarf (height 4 feet, 6 inches, weight 150 pounds). This woman had been married to her present husband four years and to a previous husband five years. Her tubes were patent. The uterus was fibrotic and retroverted. The lowest coital frequency reported was once in every two or three months. This woman had also been married previously. The reproductive organs were hypoplastic and she had twice conceived and aborted spontaneously. Her present husband's semen was found to contain actively motile sperm. Following treatment and coital instruction she conceived and gave birth to a normal child.

One hundred and fifty-five women attempted to evaluate their sexual desire; 108 (69 per cent) considered themselves normal in that respect, 41 (27 per cent) claimed to be frigid, and 6 (4 per cent) thought their libido greater than average.

Seventy-eight per cent of these wives stated that no measures had ever been employed to prevent conception since their marriage. Twenty per cent said they had practiced contraception (douche, condom, or withdrawal) early in their married lives but had discontinued it when they desired a child. Two women had relied upon a "gold ring" pessary inserted in the uterus. They reported 5 and 2 spontaneous abortions, respectively.

On admittance to the clinic, 25 per cent of the patients were found to be overweight, 24 per cent underweight, and 51 per cent within normal limits for their ages and heights. There was no significant difference between primary and secondary sterility groups in this respect.

The principal pathologic conditions discovered at the time of the preliminary pelvic examination are listed according to frequency of occurrence in Table II.

TABLE II. ASSOCIATED PELVIC PATHOLOGY IN 483 CASES OF STERILITY

	TOTAL	%	PRIMARY STERILITY	%	SECONDARY STERILITY	%
No pathology	32	7.0	11	4.0	21	10.5
Adnexal pathology	280	58.0	167	59.0	113	57.0
Endocervicitis	230	48.0	139	49.0	91	46.0
Erosion	149	30.0	76	27.0	73	37.0
Retroversion	148	30.0	91	32.0	57	28.0
Infantilism	126	26.0	95	33.0	31	15.0
Fibroid uterus	52	11.0	34	12.0	18	9.0
Stenosis of cervix	16	3.0	11	4.0	5	2.0
Bicornuate uterus	3	0.6	3	1.0	--	--
Cervical polyp	3	0.6	2	0.7	1	0.5

It is rather surprising to review the relative incidence of the various types of pathology and to note how, with two notable exceptions, it varies little with the history of previous conceptions. Cervical erosion

occurred with greater frequency in those who had previously undergone childbirth or abortion while hypoplastic genitals were more often seen in those who had never conceived; but, in the majority, the two groups showed strikingly little difference. The much greater incidence of all types of pelvic pathology in our series as compared to that in Kotz and Parker's[1] group of private patients may be possibly and partially explained by the variants of economic status and medical care in the two groups. The above investigators found an average of but 2.5 sterility factors per couple, while we report 3.3 sterility factors. Meaker and Vose,[2] in a thorough study, report 4.8 factors in sterile unions. When one considers the type of patient encountered at Bellevue, we are certain that if we had been able to include detailed etiologic studies of the husbands, the number of sterility factors per couple would have been much higher.

Semen specimens were examined in 364 cases. In 54 (15 per cent) no spermatozoa were found (azoospermia). Dead sperm only (necrospermia) appeared in 5 per cent of the cases. In an additional 29 per cent of this group the semen showed some type of abnormality which was serious enough to warrant the classification of "infertile," 85 (23 per cent) specimens were considered to be "borderline" to "fair," while only 102 (28 per cent) samples appeared microscopically adequate so as to be pronounced definitely "fertile."

In many cases the patient left the clinic before the existing contraindications to a safe Rubin test could be eliminated. In some the pathology was too extensive ever to warrant insufflation.

The Rubin test was performed, however, one or more times in 275 cases. At the initial test, 158 (57 per cent) patients were found to have bilaterally patent tubes, 109 (39 per cent) patients with bilaterally nonpatent tubes, while in 8 (4 per cent) patients the tubes were reported as partially obstructed. Uterograms were made in 83 of the 275 cases. In 75 (93 per cent) cases the roentgenograms confirmed the Rubin test; in 8 (7 per cent) patients it was contradictory. In 4 of the latter group the Rubin test was subsequently proved correct (conception occurred).

Following repeated insufflation, 37 (34 per cent) of the 109 patients in whom the first test showed negative results, were found to have patent tubes and, of this group of 37 patients, 6 women (16 per cent) subsequently became pregnant.

The basal metabolism test, although considered highly desirable as a routine, was, due to limitations of facilities, actually performed in only 133 patients. Eighteen patients (16 per cent) were found to have basal metabolic rates below minus 10, while 23 patients (20 per cent) were found to have basal rates above plus 10. The basal metabolism rates of the primary and secondary sterility groups differed in that the latter presented a greater incidence of readings above plus 10 (31 per cent to but 13 per cent below minus 10). In primary sterility the incidence of elevated and subnormal basal readings differed much less, being 13 and 17 per cent, respectively. The difference in the two groups is more strikingly brought out by comparing the proportion of cases falling above and below the 0 point; among the patients who had

never conceived there were exactly 50 per cent on the plus side and 50 per cent on the minus side, while among those who had previously reported pregnancies, 61 per cent were above the zero point and 39 per cent were below it.

In 156 cases (32 per cent), sterility was considered absolute, due to the presence of azoospermia or closed tubes or both. This figure is in exact accord with that found by Meaker and Vose.[3]

The female partner was found to bear the responsible sterility factor in 253 (52 per cent) of our cases; the male alone in only 10 cases (2 per cent). Both partners were considered infertile in 206 (43 per cent) records. It is highly probable that the relative number of cases of divided responsibility would have been greatly increased if we could have examined the semen of all the male partners, since in nearly one-half of those wherein the wife was considered as infertile, the reproductive status of the husband was unknown. In 3 per cent of the total group no explanation for the failure to conceive was found. Indeed 6 individuals of this small subseries of 14 became pregnant while undergoing investigation.

In the entire series of 483 patients, 74 women (15 per cent) conceived to our knowledge. As already pointed out our follow-up was inadequate. Rarely do the clinic patients who achieve successful treatment feel called upon to report spontaneously their success. Inasmuch as the majority of the known conceptions were traced only through chance follow-up, we feel justified in our belief that other conceptions probably occurred which were not called to our attention. Nevertheless, the known cases of successfully treated sterility may be classified as follows: pregnancy occurred in 43 women (21 per cent) of those 209 individuals in whom the treatment of their sterility was considered to be potentially successful. This group included women with known tubal patency but whose mates disclosed apparent semen defects (short of azoospermia). In the 274 women in whom the prognosis for relief of their sterility was deemed to be poor, it was evinced that 21 individuals (11 per cent) subsequently were impregnated.

In but one case of the group of 43, in whom the prognosis for cure of sterility was considered hopeless, was the outcome of treatment successful. Two major factors militated against hope of pregnancy in this case, a negative Rubin test and a husband who exhibited inactive sperm. In this case the use of iodized oil, for an uterogram, following a previous Rubin test, revealed a patent right oviduct. This patient subsequently delivered two living children.

Nine patients who presented nonpatent tubes upon their admittance but who were mated to males with actively motile sperm, eventually became pregnant; while 21 cases exhibiting patent tubes but whose husbands gave suggestions of infertility, conceived. The prognosis for satisfactory treatment of sterility was somewhat better in the secondary sterility group (19 per cent) than in those having primary sterility (13 per cent). This was anticipated, as a greater relative number of cases (62 per cent) having an unfavorable prognosis were in the latter group than in the former.

Age of the women as an etiologic factor bore little significance in this series of sterility cases. Fifteen per cent of those patients under the age of 30 years and 12 per cent of those beyond that age ultimately conceived. Duration of marriage appeared to be a more significant factor: 18 per cent of women married less than five years became pregnant, while only 12 per cent of those married a longer time were rewarded by conceptions.

In the 74 patients who conceived, a total of 83 pregnancies occurred. Of these pregnancies, 19, more than one-fourth, terminated in spontaneous abortion, while a single gestation, being extrauterine, required salpingectomy.

Since the termination of this study an attempt has been made to follow our sterility patients through the early months of gestation. Corpus luteum hormone and vitamin E were administered to those who seemed inclined to abort. The data of this experience are not yet ready for publication.

SUMMARY

The records of 483 consecutive cases admitted to the Sterility Clinic of Bellevue Hospital have been analyzed for factors which were thought to have a probable bearing upon reproductive inadequacy.

An average of 3.3 "sterility factors" for each couple was found. This figure would undoubtedly have been higher if more extensive study of the male partners of our patients had been made.

The absolute and relative frequencies of the various factors found upon admittance are noted and discussed. The factors which seemed to be associated most positively with sterility in this series were adnexal pathology (both with and without obstruction of the Fallopian tubes), endocervicitis, seminal abnormalities, abnormalities of basal metabolic rate (deviations above and below the accepted norm), and duration of marriage.

The author wishes to express her appreciation to Dr. H. Harold Lardaro, Chief of the Sterility Clinic, for his cooperation, without which this study would not have been possible.

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McCorkle, H. J., and Bell, H. Glenn: Hydrocele of the Femoral Hernial Sac, Ann. Surg. **113**: 264, 1941.

The authors stress the rarity of this condition and furnish the histories of three proved cases of their own. The factors involved in the formation of femoral hydrocele are mentioned. The presence of a potential or actual femoral hernial sac or an embryologic rest aids in the explanation of the presence of femoral hydrocele. The fluid can either come from the peritoneal cavity when there is a definite communication or by inflammation within the sac or by trauma. The latter are merely theoretical possibilities.

William Berman

NECROSIS OR THROMBOSIS IN THE ABNORMALLY BLEEDING ENDOMETRIUM?

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LOCALIZED areas of necrosis have not infrequently been described in hyperplastic endometriums. Although several textbooks of gynecologic pathology[6c, 15, 11b] refer to a necrotic process in the descriptions of abnormal endometriums, it is omitted in other well-known monographs.[5, 7]

In 1900 Cullen[3] demonstrated localized areas of necrosis in the hyperplastic endometrium. Fifteen years later, R. Schroeder,[12] in his classical paper on menstruation, emphasized the frequency of these patches in such endometriums and ascribed to the necrotic changes an important role in the vascular mechanism of abnormal bleeding. Subsequent investigators[2, 3, 6a, 6b, 14, 16] concurred with Schroeder on the frequency and probable significance of this observation. These lesions were found less frequently by Novak,[11a] who minimized their importance as a source of profuse bleeding, and regarded them as a result and not a cause of hemorrhage.

Robert Meyer[10] has been impressed with the frequent association of endometrial necrosis, stromal hemorrhage, and thrombosis of capillaries in cases of endometrial hyperplasia, but apparently reached no conclusion with regard to the necrosis.

In a series of cases of functional uterine bleeding, Fluhmann[6a] reported necrotic changes in 39 per cent of cases where the specimen was obtained while the patient was actually bleeding, and only in 0.05 per cent of nonbleeding cases. In a series of cases of endometrial hyperplasia,[6b] he encountered necrosis in 43 per cent of actively bleeding patients and only in 2 per cent of quiescent patients.

MATERIAL FOR STUDY

All uteri and curettings received in the laboratory of the Beth Israel Hospital during 1940 and the first three months of 1941 were examined histologically (hematoxylin-eosin). Cases of pregnancy, malignant tumors, and infections were excluded from the study. There were 243 uteri and 136 curettings in this series.

From two uteri, representative blocks of tissue were cut in serial section and stained with hematoxylin-eosin and the Bielschowsky silver stain.

1. HISTOLOGIC PICTURE OF ENDOMETRIAL "NECROSIS"

The "necrotic" patches are distributed irregularly in the upper layers and on the surface of the endometrium (Figs. 1 and 2), except when they occur in adenomyotic structures. They appear as variously-sized and irregularly-shaped patches and stain a light pink to pinkish gray with hematoxylin-eosin. When such foci appear above a mucosal surface, whose continuity has been destroyed in the process of shedding, they are partly or completely encircled by a collar of stromal cells. Embedded within these homogeneous, hyaline-like plaques are leucocytes, free nuclei, and occasionally a few red blood cells (Figs. 2 and 3).

The endometrium, which harbors these changes, is striking, particularly the vascular components. Capillaries appear numerous, dilated, filled with red blood

cells, and are distributed throughout basalis and functionalis. Very often, capillary dilatation is extreme with formation of large venous sinuses, especially in the upper layers. Thrombosed capillaries and thrombosed venous sinuses make their appearance as the surface of the endometrium is approached. Invariably, such endometriums show leucocytes and hemorrhage in the stroma. The mucosal surface frequently has a ragged and moth-eaten appearance.

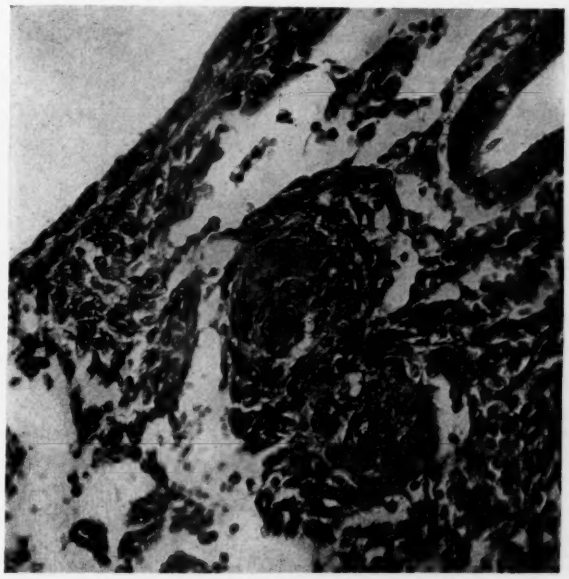

Fig. 1.—Thrombotic plaque in upper layer of endometrium. No vessel wall can be seen at the edge of the plaque. The intact surface epithelium runs across the left upper edge of the picture. The empty spaces surrounding the plaque probably are artifacts.

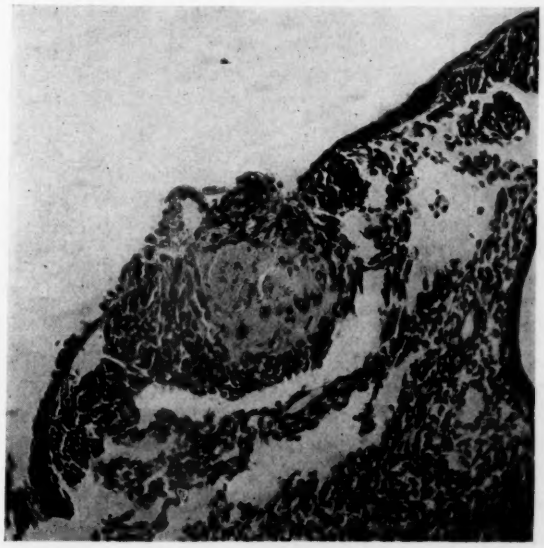

Fig. 2.—Small thrombotic plaque protruding from endometrial surface.

2. WHAT IS THE MECHANISM IN THE FORMATION OF THESE PLAQUES?

The sequence of events, as deducted from the study of the sections, appears as follows:

Dilated, blood-filled capillaries become thrombosed. The thrombi undergo hyalinization. As the surface of the endometrium is approached, the wall of the thrombosed capillary disappears, either partially or completely (Fig. 3). The end-

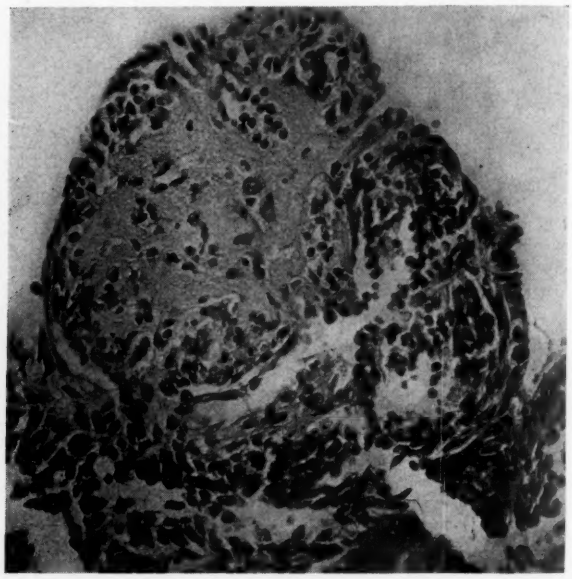

Fig. 3.—Thrombotic plaque; medium magnification. The original vessel wall cannot be recognized.

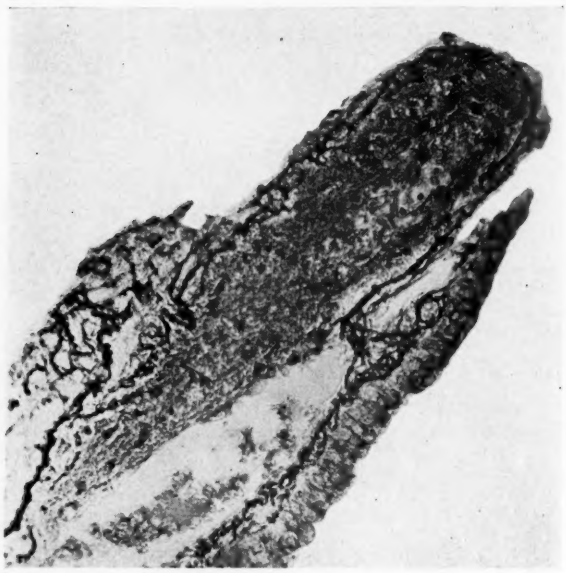

Fig. 4.—Thrombotic plaque. (Bielschowsky silver stain.) Remnants of the capillary wall can be seen.

result is a homogeneous, irregularly-shaped, light pink to pinkish gray patch, as described, or an area hardly absorbing any eosin. When patches, due to shedding, are situated above the mucosal surface, they are partly or completely enveloped by stromal cells, and even in this location an occasional strip of the previous capillary wall may be seen to hug some aspect of the margin of the patch (Fig. 4). The plaques which were studied in serial section revealed continuity with a blood vessel.

In no instance was any perivascular necrosis seen. At the surface of the endometrium, where the plaques are most usually encountered, there is a disintegration of the stromal and glandular components, a mechanical breaking-up of these tissues. Careful study of these bits of tissue always revealed intact cells. There was no histologic evidence of a necrobiotic process.

3. STUDY OF 243 UTERI AND 136 CURETTINGS

Thrombotic plaques* were encountered in 62 cases (34 curettings and 28 uteri). They were seen approximately twice as often in curettings as in the extirpated uteri (Table I). In this group of 62 cases, the endometrium was hyperplastic in 34 (Table I), and a history of abnormal bleeding was obtained in 60 cases.

TABLE I. PHASE OF SPECIMENS CONTAINING THROMBOTIC PLAQUES

ENDOMETRIUM	UTERI, 28 CASES	CURETTINGS, 34 CASES
Proliferative	1	3
Secretory	1	2
Atrophic	5	9
Hyperplastic	19	15
Mixed	2	5

In the entire series of 406 specimens, there were 74 instances of endometrial hyperplasia. Of this group of 74 cases, thrombotic plaques were encountered in 34. In the remaining 40 cases of endometrial hyperplasia in which thrombotic plaques were not seen, 32 showed varying degrees of stasis, stromal hemorrhage, leucocytic infiltration, and 26 presented a history of abnormal uterine bleeding.

At no time were sections containing thrombotic plaques or thrombosed vessels seen in the absence of stromal hemorrhage.

Of this collection of 406 cases, we were able to obtain information as to whether the patient was actually bleeding at the time of operation in only 43 cases (mostly from the year 1941). The importance of such data has been emphasized by Fluhmann.[6a, 6b] In this group of 43 cases, thrombotic plaques were observed in 26, and of these, 22 occurred in hyperplastic endometriums (Table II).

TABLE II. CASES WITH UTERINE BLEEDING AT TIME OF OPERATION

	PROLIFERATIVE	SECRETORY	ATROPHIC	HYPERPLASTIC	MIXED
Thrombotic plaques found	1	0	2	22	1
Thrombotic plaques not found	1	1	3	11	1

The uteri which contained thrombotic plaques were the seat of other lesions as follows:

Internal adenomyosis	8 cases
Myomas	15 cases
Hyperplasia of myometrium	2 cases
Myomas and internal adenomyosis	20 cases

*The term, "thrombotic plaque," is employed in contradistinction to an easily recognizable, intraluminal thrombus.

The frequent association of a thrombotic process in the endometrium with myoma and internal adenomyosis seems impressive. It appears less striking, however, when one considers that the indication for hysterectomy, in a majority of the cases, was a myomatous uterus, and that the uteri of the numerous curettings examined were usually normal or not sufficiently diseased to warrant removal.

Due to paucity of material, a study of associated ovarian disease was not attempted.

DISCUSSION

What have previously been regarded as localized areas of necrosis in the endometrium represent areas of capillary thrombosis, with partial or complete loss of the vessel walls, with progressive hyaline-like change of the thrombi, and a mechanical disintegration of the stroma. The breaking up of stromal and glandular components is not the result of a necrotic process, since no evidence of necrosis could be found. It may, in part, be attributed to the mechanical action of stromal hemorrhage, which is a concomitant feature of those cases. The elevation and detachment of masses of necrotic endometrial tissue by hemorrhage, followed by fissuring, as occurs during menstruation, was not observed in those endometriums in which thrombotic plaques were demonstrated.

Previous observers have called attention to the association of thrombosed capillaries and localized "necrosis" of the endometrium. R. Schroeder[12] postulated that these areas represent infarction due to thrombosis of vessels. Such a concept has been favored by others.[2, 6a, 13, 16] In this study we could not demonstrate the accepted criteria for infarction.

Apparently Teacher[15] did not regard these plaques as areas of necrosis. He studied them in serial sections and concluded that they were either thrombi, or the blob of a thrombus-like, slowly formed clot, which gathered around the end of a ruptured blood vessel and probably arrested the hemorrhage. Teacher has been impressed by the large, thin-walled vessels and general venous congestion of these endometriums, but was unable to express a definite opinion on the relation of this vascular picture to hemorrhage. He has described the surface stroma adjacent to the thrombotic plaques as "degenerative."

Necrosis does occur during menstruation.[1, 9] Thrombosis, which is so conspicuous a feature in the hyperplastic endometrium and other types of endometriums given to abnormal bleeding, apparently does not occur during menstruation. It was not observed in Markee's brilliant experiments[9] and was not alluded to in the exhaustive accounts on menstruation by Bartelmez.[1a, 1b] This suggests that the vascular mechanism of bleeding is altered in those endometriums which are the seat of thrombosis. The demonstration of thrombosis and of necrosis-like foci in endometrial hyperplasia induced in the castrated macaque by daily injections of estrone[17] supports such a thesis. The evidence that has accumulated in favor of the popular "withdrawal" theory in estrogenic bleeding[8] points in the same direction.

The most conspicuous feature of the endometrium, victim of thrombosis, as observed in this study, is capillary dilatation and capillary

stasis. Since vasoconstriction and vasodilatation play such vital roles in the normal bleeding mechanism,[9] some aberration of this rhythm probably occurs in those cases which exhibit thrombotic phenomena, particularly since the available evidence does not disclose thrombosis to be a feature of normal menstruation, and since the uteri, which contain thrombi, bleed abnormally. The thrombosis is, most likely, a result and not a cause of the profuse bleeding often seen in such cases, for thrombosis was never seen in the absence of hemorrhage, and yet hemorrhage was frequently observed in the absence of thrombosis.

Markee[9] has shown in the macaque that a few days prior to the onset of menstrual bleeding a phase of vasodilatation or stasis occurs. This is followed by vasoconstriction, which begins within twenty-four hours before the onset of bleeding. When a constricted artery relaxes, hemorrhage ensues. Bleeding ceases promptly when that artery is again constricted.

These observations, combined with our findings, might lead to the following theoretical considerations: The cycle is arrested during a phase of vasodilatation or stasis, or the vasodilatory phase of the regression stage is prolonged. This is followed by vasoconstriction of sufficient duration to produce damage to the capillary bed. With the release of the Daron[4] Type 1 arteries, bleeding begins. Tamponage effect (vasoconstriction) then takes place and bleeding ceases. Oozing continues from the engorged, injured capillary bed until the capillaries become thrombosed. An objection to such a hypothesis is that only about 25 per cent of the blood lost during menstruation is of venous origin.[9]

CONCLUSIONS

1. Areas previously regarded as necroses in hyperplastic endometriums represent thrombotic, hyalinized plaques, minus the vascular coat. They are embedded in a disintegrated but nonnecrotic stroma.
2. These foci are confined to endometriums which bleed abnormally, and are most frequent in the hyperplastic endometrium. They can be demonstrated if the specimen is obtained during, or immediately after, a bleeding episode.
3. Thrombotic phenomena are pathologic in the endometrium.
4. Correlation of this study with Markee's observations of the menstrual mechanism in the macaque is attempted and a hypothesis proposed.

I am deeply indebted to Dr. Alfred Plaut for his constant guidance and helpful criticisms.

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HORMONE MANAGEMENT OF THE NAUSEA AND VOMITING OF EARLY PREGNANCY

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SO MANY of the pathologic conditions associated with pregnancy are evidences of hormonal dysfunction that we were tempted to apply the hormone key to the nausea and vomiting of early pregnancy, a condition that has long been regarded as a "toxemia."

Hawkinson[1] has already reported excellent results in these cases following the administration of estrogens, and Freeman, Melick and McClusky,[2] and Kotz and Kaufman[3] have published equally good results ascribed to adrenal cortex extract. Bandstrup[4] has been more cautious in recommending the latter, but admits that it undoubtedly cures certain patients with hyperemesis. Sussman[5] has advocated parathyroid extract together with calcium, and Falls[6] has used Lugol's iodine on the ground that many such patients display a transient hyperthyroidism.

METHOD

I routinely do blood estrogen determinations[7] on antenatal patients as they present themselves. Clinically identical nausea and vomiting have been observed in both those with positive (high) and those with negative (normal or low) estrogen values, and therefore I have been disinclined to adopt the estrogen treatment of Hawkinson for all vomiting pregnant patients. It has seemed more logical to give estrogens to those with negative tests and an antiestrogen to those with positive tests. The antiestrogen selected has been testosterone propionate. It has proved much more efficacious than such antiestrogens as wheat germ oil or progesterone. Prolan preparations have not been tried. Where estrogens were used they were given in 10,000 international unit doses hypodermically every three days, if required by symptoms, and tablets were substituted as soon as feasible. When testosterone propionate was used it was given in 10 mg. doses similarly spaced, and in one of our recent successful cases the oral form was used.

DATA

The cases were grouped approximately according to the plan used by Kotz and Kaufman, as follows:

Group A represents nausea and occasional vomiting.

Group B represents daily nausea and vomiting (occurring once or oftener each day).

Group C represents vomiting of all food.

Group D represents true hyperemesis, with the output greater than the intake.

GROUP	NUMBER OF CASES	BLOOD ESTROGEN VALUES	THERAPY	AVERAGE NUMBER OF TREATMENTS	RESULTS		
					CURE	HELP	NO HELP
A	13	8 (plus) 5 (minus)	Testosterone estrogen	4 hypodermics 2 hypos then tablets	5 3	2 2	1 0
B	25	17 (plus) 8 (minus)	Testosterone estrogen	5 hypodermics 2 hypos then tablets	13 6	3 1	1 1
C	8	8 (plus)	Testosterone	4 hypodermics	8	0	0
D	4	2 (plus) 2 (minus)	Testosterone estrogen	3 hypodermics 3 hypos then tablets	2 2	0 0	0 0
Total	50	35 (plus) 15 (minus)	As above	As above	39	8	3

DISCUSSION

Widely varying types of treatment have been recommended in the literature for vomiting in early pregnancy and, surprisingly, each seems to help certain patients. Many of the women in our series had had prior trials of the usual sedatives, as well as frequent dry feedings, isolation and bed rest without any favorable effect being observed. On the other hand, three of the four patients in Class D and one in Class B did not react favorably to our treatment until they were hospitalized, when the identical therapy became effective immediately. One cannot completely discount the psychogenic factor in pregnancy vomiting, therefore. That the results achieved were not due entirely to psychic factors is demonstrated by the fact that sometimes an attempt was made to initiate hypodermic treatment, the drug used being based upon clinical judgment only, before the blood estrogen values had been reported. Where these clinical judgments proved to be incorrect in the light of the laboratory assay no help was obtained. When the assay report finally did come back and the more appropriate alternative substance was used hypodermically its beneficial influence became apparent at once, although the patient was not told that the treatment had been modified and of course had no way of knowing that such was the case. This fact seems to emphasize that there is no simple clinical method of accurately deciding to which type a patient belongs, for the symptoms are identical in high and low estrin types. It should also be noted that patients who resented hypodermic treatments highly insisted that they were much preferable to the vomiting they had experienced before such therapy had been instituted, and accordingly continued treatment until it became necessary no longer.

No explanation of the therapeutic effect obtained is attempted beyond the vague impression one gathers that the ship of pregnancy sails the estrogenic sea best at slack tide.

SUMMARY

1. Thirty-five patients with vomiting in early pregnancy were treated with testosterone propionate because they exhibited high blood estrogen levels; of these 80 per cent were cured and 14 per cent greatly helped.

2. Fifteen cases clinically identical, but with low or normal blood estrogen levels, were treated with estrogens; of these 73 per cent were cured and 20 per cent were much helped.

The author thanks Schering (Limited) of Canada for the supplies of progynon B, progynon DH, and oretone used in these clinical trials.

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A TWENTY-FOUR-HOUR PREGNANCY TEST

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FEW will disagree with Crew, of Edinburgh, when he states that, "among the instruments of precision that medicine has devised and used in the execution of its purposes and ideals, there is none finer than the biologic test for early pregnancy. Its value to the profession, to the general public and to the state . . .'"[1] is fully accepted.

A pregnancy test, to be of real value, must be correct in 98 to 99 per cent. Such accuracy had been attained in our laboratory when, in 1934,[2] we reported 1,093 Friedman tests of intrauterine pregnancy which showed false negatives in 0.55 per cent, and false positives in 0.09 per cent.* To date the Friedman tests have reached 3,063 with 0.03 per cent false positives. In 1934 we pointed out that 3.4 per cent of rabbits proved refractory. The present data based on 3,063 tests show that of 2,116 rabbits used in "positive" urines, 134, or 6.3 per cent, proved refractory. This, therefore, further emphasizes our previous insistence that it is *essential to use two rabbits for each test.*

Numerous incorrect reports have come to our attention, emanating mainly from small neighborhood laboratories and from tests made by physicians who keep a few rabbits in their offices. Investigation has convinced us that the high cost of rabbits, the space required for housing them, the necessity of isolation for three to four weeks between tests if the animals are to be used repeatedly, in other words economic factors, account for the use of only one animal. In the hope of reducing the expense involved in performing a test for pregnancy, we have experi-

*The results in extrauterine pregnancy, for reasons which we then discussed,[2] are of value only if positive.

mented since January, 1940, and have now evolved a technique which not only reduces the cost to one-quarter of the rabbit test but likewise shortens the time from forty-eight to twenty-four hours.

In addition to the Aschheim-Zondek test, which requires 5 mice and the elapse of ninety-six hours in time, and the Friedman test, requiring 2 rabbits and forty-eight hours in time, various other tests have been proposed. None of these, with one exception, approach the requisite accuracy. Among the proposed tests were the estrin, the fish tests, the allergic skin tests as well as the chemical tests, none of which have proved reliable.[3] The sole other test that appears dependable is based upon the injection of pregnancy urine into the lymph sac of the South African frog *(Xenopus laevis)*[4] which is followed in six to eight hours by the deposit of ova within the cloaca. This frog, however, is not available generally in this country.

The test which we present, in essence, is a modification of the Aschheim-Zondek test, two rats being employed instead of five mice, with reduction in time from ninety-six to twenty-four hours.

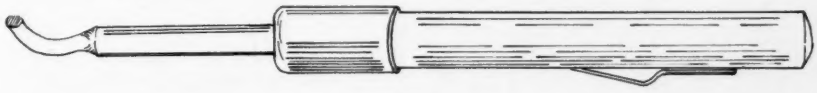

Fig. 1.

TECHNIQUE

Animals Used.—Two immature white female rats, each weighing 50 Gm., are employed. We use the Sherman strain albino but the Long-Evans strain has been found to react equally well.

Whenever possible, the first morning voided urine is used. Sediment is removed by centrifugation; urine is kept in refrigerator at 40° F. Before injection, allow urine to stand at room temperature for one-half hour to remove chill.

Injection.—Each rat received 10 c.c. of urine. Five cubic centimeters are injected subcutaneously under the loose skin of the back at 10 A.M. and the remaining 5 c.c. at 4 P.M.

The animals are killed the next morning (twenty to twenty-four hours after the first injection) with illuminating gas or chloroform. The abdomen is opened, and the ovaries removed with fine scissors and forceps, without traumatizing them. The ovarian bursa and tube are dissected away.

Readings.—Ovarian readings can be made by gross inspection.

Negative ovaries are small, pale, cream colored; the surface shows minute colorless follicles.

Positive ovaries usually are enlarged 3 to 4 times. Throughout, the ovary has a definite "blush." A few or many pinkish to red-capped follicles are noted.

Lucite Readings.—Further and more precise confirmation is obtained by examining the ovary by transmitted light with loupe magnification. The entire armamentarium consists of a small, curved, throat lucite rod, attached to a battery handle (see Fig. 1). The end of the lucite is filed off flat and then polished with fine emery paper. The ovary to be examined is lightly placed on the tip of the lucite rod without crushing its substance, and the light turned on. It is viewed through a 10 X Coddington Loupe.

Negative ovaries appear uniformly pale and cream colored. Not infrequently small red arteries are noted with no definite relation to the follicles. Here and there, between the follicles, a very faint pinkish tinge appears.

Positive ovaries.—The entire ovary presents a bright red haze. The majority of follicles are surrounded by a brilliant red zone and their surfaces covered by a minute capillary network, running toward the cap of the follicle. With the 10 diameter enlargement, the capillary network resolves clearly, the follicle then resembling the congested scleral conjunctiva of an inflamed eye (en miniature).

ANATOMIC BASIS FOR THE TEST

Sections of positive twenty-four-hour ovaries show that the characteristic hyperemic zone is due to hyperplasia of the theca interna cells with marked multiplication and dilatation of the ingrowing capillaries.

Luteinization does not occur until forty-eight hours have elapsed, a fact of which we assured ourselves by performing 105 other tests and killing the animals after forty-eight hours. Fifty-six of these tests were positive and 49 negative, all agreeing with the clinical facts or parallel Friedman tests.

TABLE I

NONPREGNANT

TYPE OF CASE	RAT TEST		RABBIT CONTROL	
	+	−	+	−
Females				
Miscellaneous	0	63	0	48
Ninth to fourteenth day of cycle	0	4	0	−
Amenorrhea	0	4	0	2
Menopause	0	6	0	3
Prepuberal	0	3	−	−
Males				
Miscellaneous	0	9	0	3
Eunuchoid	0	1	−	−
Prepuberal	0	2	−	−
Pemphigus	0	1	0	1
Pituitary tumor	0	2	−	−
Adrenal cortical carcinoma	0	2	0	1
Totals	0	97	0	58

PREGNANT

DURATION OF PREGNANCY	RAT TEST		RABBIT CONTROL	
	+	−	+	−
Unknown	16	0	15	0
10 days	1	0	1	0
19 days	1	0	−	−
21 days	4	0	1	0
4-6 weeks	10	0	6	0
6-9 weeks	21	0	11	0
9-11 weeks	6	0	2	0
11-15 weeks	13	0	4	0
20-30 weeks	18	0	0	−
30-40 weeks	10	0	−	1(?)*
Totals	100		40	1(?)

Two cases could not be classified and must be regarded as doubtful because clinical outcome proved indecisive.

Case I: Overdue 2 days; urine gave positive rat test with 10 and 8 c.c.; no further urine available. She bled next day.

Case II: One episode of irregular bleeding, ectopic pregnancy suspected; 1 rat positive, 1 rat negative, 1 rabbit (no more urine available) negative; next day's urine negative in 2 rats and 2 rabbits.

Case III: Ectopic pregnancy, eighth week. Positive reaction. Findings confirmed by operation.

*Patient in whom x-ray abortion was being induced. Gave positive rat, doubtful rabbit reaction.

To date we have performed 201 tests by the twenty-four-hour technique described above. Of these, 97 gave negative, and 104 positive results. Detailed analysis of the findings is presented in Table I. In 98 cases, parallel Friedman tests were performed because the clinical course could not be followed. The rats used were given numbers and autopsy results recorded before the case histories were identified in order to eliminate prejudgment.

DISCUSSION

Analysis of our results has shown that the reliability of the test equals that of the original Aschheim-Zondek technique and is slightly more delicate than the Friedman test. Because of this, it was imperative to obtain a sufficient number of control cases in order to eliminate the possibility of false positives due to the presence of gonadotropic factors in the nonpregnant. The urine of normal women between the ninth and the fourteenth day of the cycle, at which time ovulation may be expected and which corresponds to the greatest accumulation of gonadotropic factors in the blood and urine,[5] gave a negative result. The urine of amenorrheic and menopause patients, in whom we had previously determined a high gonadotropic titer, likewise proved negative. Two urines from patients suffering with pituitary adenomas and two from patients with adrenocortical carcinoma, gave negative responses. The urines of children of both sexes before puberty likewise were negative.

A case of uterine chorioepithelioma gave positive results with as little as 0.05 c.c. of urine. In a normal pregnancy of eight weeks' duration, at which time the gonadotropic factors reach their peak, 0.1 c.c. of urine gave a positive reading; at twelve weeks positive tests were obtained with 0.2 c.c. Nevertheless 10 c.c. was selected for the test as even at that high level, 3.1 per cent of the rats proved refractory and no false positives were obtained in the absence of gestation.

The patients upon whom these tests were made, with the exception of a few private patients whose urines were sent in without data and on which a Friedman test was simultaneously performed as a control, have all been followed so that any discrepancy between the tests and the clinical course would become apparent. The few discrepancies are analyzed as footnotes to the chart.

As 10 c.c. of urine is a large dose for a 50 Gm. rat, it is necessary to obtain the urines fresh and to avoid chilling the animal, as previously mentioned. Stale urines prove lethal even when detoxified by ether extraction, as originally recommended by Zondek. Before this was noted, 8 per cent of the rats died, which, if anything, compares favorably with the more than 3,000 Friedman tests performed, in which 9.3 per cent of the rabbits were killed by the injection. Urines from patients receiving sulphanilamide or allied drugs proved lethal to the rats. We again repeat that it is *imperative to use 2 rats for every test* as at least 3.8 per cent have proved refractory.

SUMMARY

1. A simple, inexpensive pregnancy test requiring only twenty-four hours is described. Its accuracy is equal to the original Aschheim-Zondek and Friedman tests.

2. Two female white rats, weighing 50 Gm. each, are required for each test.

3. Five cubic centimeters of fresh urine are injected at 10 A.M. and 4 P.M. of the same day; the animals are autopsied at 9 A.M. of the next day.

4. The readings are made macroscopically and with 10 loupe enlargement by transmitted light.

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ADDENDUM

Since the acceptance of the manuscript, 32 additional twenty-four-hour pregnancy tests have been performed. Clinically all of these proved correct. Seventeen of the patients proved nonpregnant, 13 pregnant. The urines of two males, at first suspected of harboring chorionepithelioma of the chest, proved negative.

In the interim, efforts have been made to shorten the test still further. By trial it was found that a positive test could be obtained in eight hours, the 5 c.c. of urine being injected at two four-hourly intervals. Twenty-seven urines from pregnant patients gave 26 positive reactions. The sole negative was the urine of a patient, thirty-two weeks pregnant, who twice gave negative readings, with a week intervening between the tests, although the twenty-four-hour readings were positive. From this it would appear that when the indications are urgent, a positive test obtained after eight hours may be relied upon.

STUDIES IN VIABILITY OF HUMAN SPERMATOZOA

Preliminary Report

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THE office determination of sperm viability is measured by their motility in a hanging drop preparation. Vigorous and progressive movement across the microscopic field is characteristic of healthy normal spermatozoa. Sluggish movements or absence of movement within one hour of the time of ejaculation is generally interpreted as a sign of lowered or absent spermatic vitality.

A better understanding of the conditions affecting sperm motility indicates that the problem of sperm vitality is not so easily solved. Factors such as viscosity, osmotic pressure, pH, temperature, oxygen concentration, all affect the metabolism of the living spermatozoa and may individually or in combination affect their motility.[1-7] Moench,[1] for example, ingeniously proved that sperms stored in the epididymis remain practically motionless due to lack of oxygen and a strongly alkaline medium, yet they are very much alive as evidenced by their activity in the ejaculate.

It would seem advisable therefore, when spermatozoa exhibit deficient or absent motility, to obtain additional information in regard to their vitality.

The procedure to be described is based on the property of living spermatozoa, like all living cells, to utilize available free oxygen. Methylene blue is used as an indicator because of its ready conversion to colorless leucomethylene blue when deprived of oxygen, and because it is nontoxic. Thus, when methylene blue is added to spermatic fluid in an anaerobic preparation, the available oxygen is utilized by the living spermatozoa. The loss of this oxygen from the preparation causes the methylene blue to change to its colorless state. On the other hand, if the spermatozoa are dead, the dye maintains its blue color because there is enough free oxygen present to prevent any change to the leuco base.

METHOD

The procedure adopted consists of placing 1 c.c. of spermatic fluid and 1/10 c.c. of methylene blue solution* in each of two ordinary Wassermann tubes. The test tubes are inverted several times to insure thorough mixing, care being taken to avoid air bubbles. A little heated vaseline is layered over the mixture by means of a

*The methylene blue is prepared as follows:

Sodium chloride	9.2 Gm.
Sodium bicarbonate	0.05 Gm.
Potassium chloride	0.1 Gm.
Calcium chloride	0.1 Gm.
Distilled water	1,000 c.c.

Dissolve the above and adjust the pH to 7.8-7.9. Then add 0.2 Gm. of methylene blue. Shake until the dye is dissolved, filter and use.

pipette. The vaseline is then permitted to harden. One test tube is placed in an incubator at 37° C. and the other test tube kept at room temperature (20° C.). Readings are taken every fifteen minutes.

The results of this experiment with 25 normal seminal specimens are charted in Table I. The semen had been collected in sterile wide-mouthed jars and was examined within one to three hours of the time of ejaculation.

Decolorization of the methylene blue was more rapid and completed earlier at 37° C. than at 20° C. At 37° C., decolorization began in fifteen minutes and was completed in one hour. Specimens kept at 20° C. began to decolorize in sixty minutes and were completely decolorized in one and one-half to two hours.

Two sets of control experiments were tried. One consisted of destroying the spermatozoa of 15 specimens by subjecting them to 65° C. for one hour before being tested by the above procedure. The other control consisted of removing the spermatozoa of 10 specimens by centrifuging at 3,000 revolutions per minute for one hour and testing the supernatant fluid according to the above procedure. All the control tubes were kept at 37° C. In every instance the methylene blue remained unchanged, showing that the spermatozoa were dead or absent (Table I).

TABLE I. RESULTS OF METHYLENE BLUE TEST FOR SPERM VIABILITY

DONOR	DECOLORIZATION TIME		CONTROLS
	INCUB. TEMP. 37½° C. MIN.	ROOM TEMP. 20° C. HR.	INCUB. TEMP. 37½° C.
1	50	1	No color change
2	40	1	No color change
3	30	1½	No color change
4	30	1¼	No color change
5	30	2	No color change
6	45	1	No color change
7	60	2	No color change
8	35	1¾	No color change
9	30	1	No color change
10	30	2	No color change
11	45	1½	No color change
12	60	1½	No color change
13	30	1¼	No color change
14	30	1	No color change
15	30	1½	No color change
16	40	1½	No color change
17	40	1½	No color change
18	30	1½	No color change
19	35	1¾	No color change
20	40	1½	No color change
21	60	1	No color change
22	35	1½	No color change
23	30	2	No color change
24	55	1	No color change
25	35	1½	No color change
Average	39	1 hr. 42 min.	

Another series of controls should also be made with seminal fluid presumed to be inadequate as to the number of spermatozoa and percentage of abnormal forms. Unfortunately these specimens were not available for study. It is likewise possible that the rate of conversion of the methylene blue to its colorless base may be significant of the degree of viability of the spermatozoa. These are problems worthy of further investigation.

SUMMARY

A simple and practical method of determining sperm viability is described, utilizing methylene blue as an indicator of the absorption of free oxygen by spermatozoa.

The authors wish to express their thanks to Dr. Harry Aranow, Director of Obstetrics at Morrisania City Hospital, and to Drs. M. J. Goodfriend and A. B. Tamis who helped in organizing the material for this paper.

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THE PORTES CESAREAN SECTION WITH REPORT OF A CASE*

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THE choice of treatment in definitely infected labor cases has been a moot question for many years. Classical cesarean section may be mentioned only to be condemned when performed upon a frankly infected case. The low cervical section with transverse cervical incision is perhaps somewhat more adaptable. Latzko introduced an extraperitoneal section, hoping it would prove to be the logical procedure in such cases. This operation, however, has great technical difficulties. Within the past year Waters[1] and Smith[2] each have suggested modifications of the Latzko procedure. Such operations, if technically not too difficult, would probably offer the greatest degree of success in the treatment of neglected individuals. These authors admit that the procedures are time consuming. In the poor surgical risk a shorter operation is advisable. The Portes type of section answers this need. It has the disadvantage of including two separate stages and a prolonged hospitalization for the patient. It has the distinct advantage of precluding the spill of infectious material into the abdominal cavity since the peritoneum is closed before the uterus is entered. This, of course, does not hold true in the Porro section wherein the uterus is removed supravaginally after the infant is extracted. Because of the more or less general debate and argument as to the proper method of handling patients exhibiting evidence of infection, it seemed worthwhile to present a brief résumé of appropriate literature on the subject together with a case report. The Portes section performed upon this woman was the first ever done in the St. Louis University Group of Hospitals.

REVIEW OF LITERATURE

In 1923 at the Maternite de Port Royal de Paris, Dr. Louis Portes first performed a cesarean section followed by temporary exteriorization of the uterus. Since that time, a number of these operations have been done in France and other foreign

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countries but only a very few in the United States. It is to be noted that the procedure is frequently referred to as the Portes-Gottschalk operation. Gottschalk of Germany described a similar technique to that of Portes as far back as 1909, but to the best of our knowledge never performed such an operation.

Phaneuf[3, 4] believes that the Portes operation is reserved for the occasional hopelessly infected patient wherein the matter of the time element is a serious consideration. This author had performed two of these procedures up to 1937, resulting in two maternal recoveries and the survival of one infant. The uterus was exteriorized for forty-one days in the case of the first patient and for thirty days in the second.

The operation itself, as described by Portes, is done in two stages. The initial portion of the procedure includes an abdominal incision, the delivery of the pregnant uterus, the closure of the abdominal wall behind the uterus down to the cervix, a high uterine incision, extraction of fetus, membranes and placenta, closure of the uterine defect allowing the uterus to remain on the abdomen, and wet packs to the wound.

The second stage follows only after the complete healing of the uterine incision and consists of re-opening the abdominal incision, freeing whatever adhesions which may have formed, dropping the uterus and adnexa back into the pelvic cavity, draining the area posterior to the uterus and closing the abdomen. Several of the French authors, however, have deemed it necessary to remove the uterus following its exteriorization owing to excessive and prolonged infection.

The mortality rate from this seemingly extensive procedure is not high considering that most cases so treated were definitely infected. Couvelaire,[5] in 1925, reported a mortality of 6.2 per cent in 32 cases. We know of Phaneuf's good results in two cases.

In 1938, Parsons[6] reported three neglected cases seen in China and treated by this method. None of the babies was living on admission to the hospital. One mother recovered and 2 died of heart failure after operation. All 3 cases showed evidence of frank infection.

DISCUSSION

Of the comparatively few authors who have written on this subject all seem to agree that the Portes operation is primarily of value in markedly infected cases wherein a Porro type of section would consume too much time. Therefore, the most important indications for the procedure seem to be neglected individuals in whom a frank infection is present and who manifestly are poor surgical risks. All authors claim a very short operative time for the Portes section, twenty-five to thirty minutes appearing to be about the average duration for completion of the first stage operation. It is, however, our impression that the procedure can be done little, if any, faster than the Porro section. We realize that practice aids in a swifter technique but the first stage operation in the case to follow required only thirty minutes. The Porro operation, in most competent hands, takes little longer and seems to us the safer procedure in the majority of cases although it must be admitted that the amputation of the uterus plus the uterine incision in this operation allows for the possible spill of infectious material into the peritoneal cavity. The case herein reported represents a 23-year-old primigravida who was just beginning her reproductive life. In this particular subject it would have been regrettable to have removed her uterus at the time of abdominal section. Therefore, since the time element is practically of no import in evaluating the Porro and Portes

techniques, we believe the general indication for the Portes type of section should include frankly infected cases in which the mother is early in her reproductive life.

In 1937, M. P. Huet[7] pointed out, in referring to the original work of Louis Portes, that the first operation of this kind was done on an infected individual, aged 21 years. Portes conceived his idea of exteriorizing the uterus because he believed that section followed by hysterectomy would have been a regrettable choice in so young a woman.

CASE REPORT

The patient, seen in Firmin Desloge Hospital on May 29, 1940, was a 23-year-old primipara whose pregnancy, until the time of labor, presented nothing unusual. Her pelvic measurements were apparently normal. The blood pressure had been moderately elevated and for this condition she had had some treatment. When first seen her temperature was 102° F. and pulse 120. The white blood cell count was 20,000 with a shift to the left in the differential. The membranes had ruptured forty-eight hours previously, and she had been in fairly strong labor for three days. The abdominal examination revealed a uterine pregnancy of approximately full term with a right position. The fetal heart tones were good in the right lower quadrant. The rectal examination revealed the presenting part, the head, high in the pelvis. It was ascertained by questioning that both the patient and her husband were desirous of future pregnancies and because of this fact and the evidence of frank infection in so young a woman, a Portes type of cesarean section was decided upon. The patient was given several vaginal instillations of an antiseptic solution and taken to the operating room where the abdomen was opened under gas anesthesia. The uterus was delivered through the incision and the peritoneum was then closed about the uterus. An incision was then made into the uterus and a full-term male infant, weighing 9 pounds 3 ounces was delivered from an R.O.P. position. The cry and respiration were spontaneous. The placenta was removed manually and a foul odor arising from the uterine cavity was noted. The uterine incision was then closed, leaving the uterus outside the abdominal cavity. The time consumed in this procedure was thirty minutes.

Following this operation the patient ran a temperature of 101 to 103° F. for several weeks. Neoprontosil was given in large amounts together with several blood transfusions. The area around the uterine wound sloughed extensively despite the presence of constantly wet saline packs. This condition finally was controlled sufficiently to permit the second stage operation fifty-five days after the original procedure.

On the twenty-fourth of July, 1940, the patient was again anesthetized, the uterus was freed from its attachments to the abdominal wall and the abdominal cavity was re-opened. The uterine fistula was closed with 2 rows of catgut sutures. The raw uterine surface was covered with bladder peritoneum and the uterus was dropped back into the pelvic cavity. The right tube was found to be patent but a probe could not be passed into the left tube. The abdomen was closed in layers. This procedure, which was made exceedingly difficult due to a retraction of the peritoneum, was completed in slightly less than two hours and was complicated only by the development of a small abdominal wall fistula which was treated by styptics and which gradually healed. The patient left the hospital on Sept. 4, 1940, exactly ninety-eight days after the initial operation. She has menstruated regularly since then and to all external evidence is in good condition.

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MENORRHAGIA AS A PRIMARY FACTOR IN VARIOUS BLOOD DYSCRASIAS

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GYNECOLOGIC symptoms of systemic disease are by no means uncommon. Menstrual disturbances, such as amenorrhea and menorrhagia, are quite characteristic of generalized cachexia due to any cause. Occasionally, however, the gynecologist is confronted with a presenting symptom so characteristically gynecologic in type that the actual etiologic factor is discovered only after extensive systemic investigation, or by the sudden exacerbation of generalized symptoms of a disease which had previously manifested itself in abnormal menstrual function only. Frank[1] has recently stated, "It is now accepted that functional diseases of the female may originate not only in the ovary, but also in the pituitary, adrenal, or thyroid glands." In addition to these endocrine factors he might have added abnormalities of the hematopoietic system, because the actual occurrence of uterine bleeding is affected by the condition of the blood vessels and the blood itself. Various blood dyscrasias, such as purpura hemorrhagica, aplastic anemia, or leucemia, ordinarily have easily identifiable diagnostic characteristics. Occasionally, however, their presenting and only symptom is menorrhagia, and it is with these latter cases that we are directly concerned.

This condition has received some attention in the literature in the form of isolated case reports, Israel and Mendell[2] having reviewed the subject in 1939 and added a case of their own. Jennings and Castleden[3] reported another case from England in the same year, but, so far as we know, there has been no attempt made to evaluate the frequency with which gynecologic abnormalities are the presenting symptoms of these disorders.

A brief review of 108 cases of purpura hemorrhagica, aplastic anemia, and leucemia taken from the record files of the Presbyterian Hospital reveals that no less than 10 of these patients presented themselves for medical treatment with a chief complaint of menorrhagia. In many other cases this gynecologic symptom occurred as one of the incidental factors in a condition already diagnosed, yet in this series an incidence of nearly 10 per cent of cases of blood dyscrasias were first seen in a gynecologic clinic or were first treated for their gynecologic complaint.

Various treatments for uterine bleeding were instituted before other systemic manifestations of the actual hematopoietic pathology presented themselves. Local treatment was carried out in 3 cases, vaginal packing being used in 1, curettage in another, and hysterectomy in a third subject. Four patients received various types of medication,

TABLE I. CASES OF BLOOD DYSCRASIA IN WHICH MENORRHAGIA WAS THE INITIAL SYMPTOM

CHART	AGE	CHIEF COMPLAINT	PREVIOUS TREATMENT	OTHER SYMPTOMS	DATE OF APPEARANCE OF OTHER SYMPTOMS AFTER ONSET OF CHIEF COMPLAINT	DIAGNOSIS	RESULT
544403	28	Menorrhagia 2 yr. Profuse 3 weeks	Vitamin C Transfusion Antuitrin	Pallor Weakness Ecchymoses	About 1 yr.	Aplastic anemia	Died
444336	54	Vaginal hemorrhage 2 yr. ago	Hysterectomy	Anemia Weakness Loss of weight	Since operation	Aplastic anemia	Died
377204	15	Menorrhagia (Functional?)		Fatigue	With chief complaint	Purpura hemorrhagica	Splenectomy
581584	21	Menorrhagia		Ecchymoses Epistaxis	With chief complaint	Purpura hemorrhagica	Splenectomy
563291	20	Menorrhagia	Dilatation and curettage	Epistaxis Bleeding from gums	3 months	Purpura hemorrhagica	Splenectomy
551210	27	Menorrhagia	Transfusion Snake venom	Ecchymoses	4 months	Purpura hemorrhagica	Splenectomy
463987	42	Menorrhagia	Ergot	None		Purpura hemorrhagica	Spontaneous Remission
77477	23	Vaginal bleeding for 7 weeks		Ecchymoses	With chief complaint	Purpura hemorrhagica	Splenectomy
482332	33	6 months' miscarriage with profuse bleeding. Menorrhagia since	Packing	Ecchymoses Epistaxis	2 months	Purpura hemorrhagica	Splenectomy
315921	18	Menorrhagia	"Pills and medicine"	Purpuric spots Bleeding gums	2 weeks	Acute lymphatic leucemia	Died

including vitamin C, chorionic gonadotropic hormone, snake venom, and ergot. Transfusions were administered to 2 of these patients. A brief outline of the history and treatment is tabulated in Table I.

CASE REPORTS

54403.—The patient was a 28-year-old female with a complaint of menorrhagia for two years with profuse uterine bleeding for three weeks. About one year after onset of menorrhagia she developed pallor, weakness, and ecchymoses. She had previously received chorionic gonadotropin therapy. A diagnosis of aplastic anemia was made, and the patient subsequently died.

444336.—A 54-year-old woman complained of profuse menorrhagia for which hysterectomy was performed. No pathology was observed in the uterus following removal. Weakness, loss of weight, and anemia became progressive following operation. A diagnosis of aplastic anemia was made. Patient died two years postoperatively.

377204.—A 15-year-old girl complained of menorrhagia which was thought to be functional in origin. Subsequent blood counts disclosed the presence of purpura hemorrhagica. Splenectomy was performed with subsequent cessation of menorrhagia.

581584.—Patient was a 21-year-old girl with chief complaint of menorrhagia. Subsequent history disclosed the presence of occasional epistaxes and ecchymotic spots. Purpura hemorrhagica was diagnosed on the basis of blood counts. Splenectomy resulted in cure.

563291.—A 20-year-old girl complained of menorrhagia. Dilatation and curettage was performed without relief, and three months later epistaxis and bleeding from gums occurred. Purpura hemorrhagica was diagnosed on the basis of blood counts. Splenectomy resulted in cure.

551210.—Patient was a 27-year-old female with chief complaint of menorrhagia. She received snake venom and transfusions without relief. Four months after onset of menorrhagia, ecchymoses appeared. Blood counts disclosed presence of purpura hemorrhagica. Splenectomy resulted in cure.

463987.—A 42-year-old woman complained of menorrhagia. She received ergot without relief and was admitted for operation. Routine blood counts disclosed presence of purpura hemorrhagica. She underwent a spontaneous remission and has been well since.

77477.—A 23-year-old girl whose chief complaint was profuse vaginal bleeding for seven weeks. Subsequent history disclosed presence of frequent ecchymoses. Purpura hemorrhagica was diagnosed on basis of blood counts. Splenectomy resulted in cure.

482332.—A 33-year-old woman had suffered a six months' miscarriage with profuse bleeding, and subsequent menometrorrhagia was unrelieved by packing. Two months later miscellaneous ecchymoses and epistaxis occurred. Diagnosis of purpura hemorrhagica was made on basis of blood counts. Splenectomy resulted in cure.

315921.—An 18-year-old girl complained of menorrhagia for which she received "pills and medicine." Two weeks later onset of menorrhagia, bleeding gums, and purpuric spots appeared. Diagnosis of acute lymphatic leucemia was made. Patient died.

SUMMARY

Ten cases of blood dyscrasias are presented whose presenting symptom was menorrhagia. Seven patients were variously treated for their gynecologic complaints before subsequent characteristics of the blood dyscrasia manifested themselves.

CONCLUSION

Although the total number of cases of uterine bleeding having occult blood dyscrasias must be relatively small, it is considered significant enough to warrant complete blood studies on every unexplained case of menorrhagia.

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AMENORRHEA DUE TO TUBERCULOUS ENDOMETRITIS

Failure of Estrogens and Progesterone to Induce Uterine Bleeding

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IT IS generally accepted that functional amenorrhea is caused by a deranged activity of the endocrine glands. The fact that the end organ, viz., the uterus, may be at fault, failing to respond to what normally would be adequate hormone stimulation, has received but scant attention in the literature. The case reported here illustrates this point, that is, the finding of tuberculous endometritis in a patient with secondary amenorrhea in whom enormous doses of estrogen and progesterone failed to induce uterine bleeding.

CASE REPORT

The patient was a 23-year-old, unmarried, nulligravida, admitted to the Ward Service on Oct. 18, 1934. Her chief complaint was amenorrhea. The past menstrual history was significant. Menses began at the age of 16 and occurred at regular twenty-eight-day intervals. The flow was scant and lasted only two days. In 1930, the menses became irregular and then stopped completely in February, 1931. In June, 1934, the patient menstruated spontaneously for four days. The past medical history was noncontributory. There was no history of contact with tuberculosis. General physical examination revealed normal findings. Pelvic examination showed an intact hymen, moist, adult type of mucosa and a uterus of normal size. The ovaries were enlarged to approximately two times the normal size. The basal metabolic rate was within normal limits.

The findings on exploratory laparotomy were a small uterus in midposition, and the right tube clubbed, slightly enlarged and adherent to a polycystic ovary 3 to 4 cm. in diameter. A moderate-sized hydrosalpinx was present on the left. The left ovary was also cystic and the same size as right. Small wedge resections were

done on each ovary. Histologic study revealed a small dermoid cyst in the section removed from the right ovary and a follicle cyst of the left ovary. Careful study of the resected tube did not reveal any evidence of tuberculosis. On the eighth day postoperatively, the patient passed grossly bloody urine and had severe epistaxis. Except for slight secondary degree anemia, blood studies were normal.

Fig. 1.—Case M. K. Endometrium obtained by suction curettage, following 372,400 R.U. of α-estradiol benzoate intramuscularly, 860,400 R.U. of α-estradiol orally, and 20 mg. of progesterone. Note atrophy of stroma; few small scattered endometrial glands. (×50.)

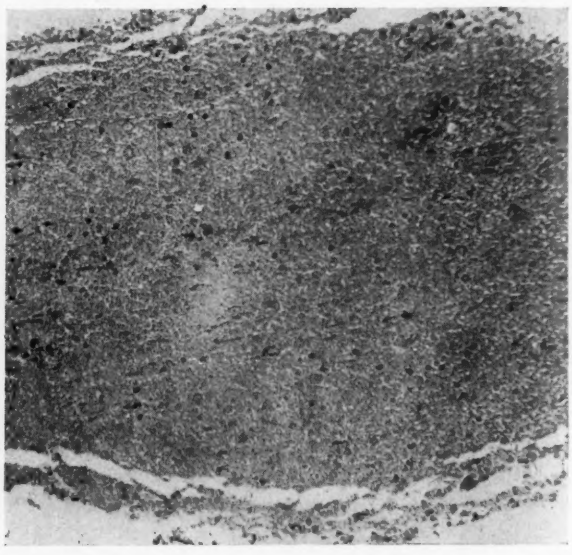

Fig. 2, *A*.—Case M. K. Endometrium following 1,028,000 R.U. of α-estradiol benzoate in oil, 860,400 R.U. of α-estradiol orally, and 120 mg. of progesterone. Note marked necrosis. (×50.)

Hemoglobin was 87 per cent; red blood cells, 3,710,000; white blood count, 8,300; platelets, 230,000; polymorphonuclears: 68 per cent nonsegmented, 1 per cent segmented, 2 per cent eosinophiles, 18 per cent lymphocytes, 9 per cent monocytes; bleeding time, one and one-half minutes; coagulation time, 11 minutes; and tourniquet test, negative. The postoperative course, thereafter, was uneventful.

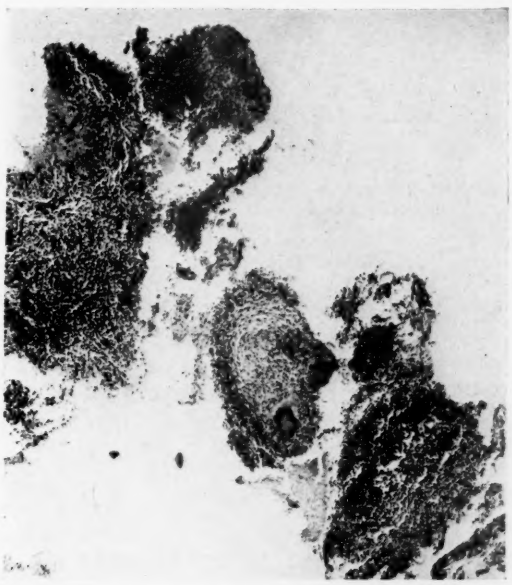

Fig. 2, *B*.—Case M. K. Another area of same biopsy showing tubercle formation with central caseation and epithelioid cells. (×50.)

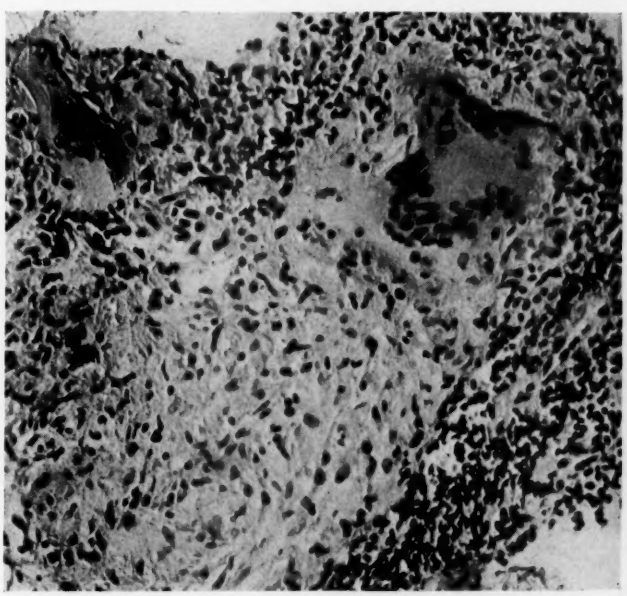

Fig. 2, *C*.—Case M. K. High power magnification of Fig. 2, *B*, revealing tubercle formation and Langhans type giant cells. (×275.)

The patient was again seen in the out-patient department in September, 1936, approximately two years following operation, complaining of vertigo, asthenia, and nervousness. There had been no uterine bleeding since operation and no flushes. However, it is noteworthy that, following operation, epistaxis had occurred at fairly regular monthly intervals. At this time, the patient was started on estrogen therapy and received continuous treatment from Dec. 6, 1937, to Aug. 15, 1938. α-Estradiol benzoate was administered 2 or 3 times weekly, in individual doses, varying from 4,000 R.U. to 10,000 R.U., supplemented by oral therapy (18,000 R.U. of α-estradiol, daily). The total dosage administered over this period of time was 372,400 R.U. of α-estradiol benzoate, intramuscularly, in addition to 860,400 R.U., orally. Without interruption of the estrogen administration, the patient was then given 20 mg. of progesterone in 5 mg. doses, over a period of two weeks, and a suction curettage was done. Only small fragments of endometrium were obtained which showed atrophy of the stroma and a few scattered glands (Fig. 1). Because of the slight evidence of estrogenic stimulation of the endometrium, we concluded that the patient had received an inadequate amount of estrogens. The dosage of estrogens was, therefore, increased to 10,000 R.U. of α-estradiol benzoate, 3 times weekly.

From Aug. 15, 1938, to Feb. 27, 1939, a total dosage of 656,000 R.U. was administered. In addition, from Jan. 30, 1939, to Feb. 27, 1939, the patient received 100 mg. of progesterone, in 10 mg. doses. In spite of the enormous doses of estrogens and progesterone, bleeding did not occur, and an endometrial biopsy by suction curettage was done.

Dr. Paul Klemperer, pathologist at the Mount Sinai Hospital, New York, described the specimen obtained as follows: "Section shows several particles of necrotic tissue (Fig. 2, *A*) in which only sporadic fragments of endometrial glands can be recognized. Some of the fragments show, in addition, slight infiltration with polynuclear leucocytes. There are other particles which show granulation tissue, including several large tubercles with caseous centers surrounded by a wreath of epithelioid cells (Fig. 2, *B*) and also tubercles including giant cells of the Langhans type (Fig. 2, *C*). The histologic picture is unmistakably that of tuberculosis, but tissue stains for tubercle bacilli were negative. (From the academic point of view, it would have been desirable to obtain fresh endometrial tissue for injection into guinea pigs in order to demonstrate tubercle bacilli. However, this was not done because of the danger of reactivating the disease.) The presence of caseation and typical tubercles is regarded as sufficient proof of the diagnosis. Furthermore, the fact cannot be denied that a severe necrotizing process has destroyed most of the endometrium."

A complete physical examination and x-ray of the chest failed to reveal any evidence of tuberculosis. The patient at the present writing has been observed for more than one year since the last endometrial biopsy. There has been no uterine bleeding and the pelvic examination remains unchanged with no clinical evidence of tuberculosis.

DISCUSSION

It is an open question whether the amenorrhea in this case was caused by the cystic disease of the ovaries, the tuberculous endometritis, or by a combination of both. The failure of the endometrium, however, to respond to the huge doses of estrogens and progesterone suggests either impairment of the normal proliferative property inherent in the endometrium and/or actual destruction of the endometrial glands and stroma, both of which are probably attributable to the tuberculous process. It has been our experience that the atrophic endometrium, even as long as thirty years after the cessation of ovarian function (spontaneous or castration), can be stimulated to a degree of proliferation and differentiation comparable to that which prevails in women with normally functioning ovaries. The dosage used in the case reported here was far in excess of the amount required to produce such a physio-

logical endometrial pattern. In view of these observations, we would advise that an endometrial biopsy be performed in all cases of functional amenorrhea prior to the institution of hormone therapy and that the presence of some destructive disease of the endometrium should be suspected if bleeding fails to occur after adequate therapy.

SUMMARY

A report has been presented of a case of secondary amenorrhea, treated with 1,028,000 R.U. of α-estradiol benzoate in oil intramuscularly, 860,400 R.U. of α-estradiol orally, and 120 mg. of progesterone, over a period of approximately fourteen months, without causing uterine bleeding. Suction curettage, following the hormone therapy, revealed atrophy of the endometrium and tuberculous endometritis. Attention is drawn to the possibility of disease of the endometrium, such as tuberculosis, causing amenorrhea by impairing the normal proliferative capacity of the endometrium or by actual destruction of the endometrial tissue. The suggestion is made that an endometrial biopsy be done in all cases of functional amenorrhea before institution of treatment and repeated if bleeding does not occur after adequate hormone therapy.

For the α-estradiol (progynon-DH) and the α-estradiol benzoate (progynon-B) used in this investigation, we are indebted to Dr. Erwin Schwenk and Dr. Max Gilbert, of the Schering Corporation, Bloomfield, N. J.

PRIMARY ENDOMETRIOSIS OF THE CERVIX UTERI

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PRIMARY intracervical endometriosis is very rare. A survey of the literature reveals only one case in which there has been direct extension of the endometrium or transplantation on the mucosal side of the cervix. The other cases that have been reported and those that we have observed have been extensions from a rectovaginal septum involvement or transplants on the posterior surface of the supravaginal portion of the cervix. We do not consider as endometriosis (endocerviosis), cases in which cervical glands penetrate deep into the fibromuscular stroma. Teacher and others have reported such cases. There is a marked variation in the normal depth of penetration of cervical glands into the fibromuscular stroma. It is obvious that erosions and lacerations with ectropion change the distribution of the endocervical tissue so that great difficulty may arise in determining whether or not it is abnormally situated or a result of invasion. At any rate the appellation is a misnomer, for the tissue does not simulate endometrium in any respect.

Rushmore, in 1931, reported an unusual case of primary endometriosis of the cervix and stated that a careful search of the literature failed to show a similar case. His patient was a young, white woman, who had been delivered by version and extraction by another physician four years previously. An immediate post-

partum hemorrhage ensued which was said to be due to the rupture of a small artery beneath the urethra. On the eighteenth post-partum day, while at home, another severe hemorrhage occurred which was controlled presumably by packing the vagina. On her first visit, four years after delivery, she complained of brownish discharge from the vagina, of one week's duration, coming on two days after the expected menstrual period was due. The patient was frightened because she thought she was suffering from ectopic pregnancy since two of her friends had recently died of that condition. Pelvic examination showed slight enlargement of the uterus and no adnexal disease. The cervix appeared normal with the exception of a small polypoid nodule about one-fourth inch in diameter, which was attached to the portio vaginalis on the right side. It was suggestive of malignancy. No discharge from the cervical canal was noted, but a slight brown discharge from the growth was observed. The growth was removed and the pathologist reported it to be composed of decidual glands and cells. The diagnosis, obviously, was an endometrial transplant which had undergone decidual formation. The patient returned in two weeks as the bleeding had continued. Pelvic examination at the time revealed the cervical growth to be two or three times its original size, and it continued to have a brownish discharge. The uterus was the size of a two and one-half to three months' pregnancy with slight enlargement in the right cornual region. A few days later an operation was done, because of the marked and unexplained change in the uterus. The endometrial implant was excised and a curettage was done. Normal tissue of an early pregnancy was removed. A laparotomy was then done and the only essential finding was a bicornuate uterus with enlargement of the right portion.

By way of explanation for this unusual occurrence Rushmore logically deduced that some endometrial tissue became lodged in a laceration of the cervix at the time of the first delivery, became embedded there and started growing.

CASE REPORT

G. C., a white woman, aged 40 years, a private patient of Dr. H. S. Crossen, was admitted to Barnes Hospital with the complaints of irregular vaginal bleeding, pain in the lower abdomen, and backache. In her past history the only relevant information was that in 1932, she had a uterine suspension, left salpingo-oophorectomy, right salpingectomy, and appendectomy. Menstruation began at 13 years of age and was regular every twenty-eight days until 1930. At that time the interval shortened to every twenty-three days and the flow lasted for seven days. Following the operation in 1932, her periods again became regular every twenty-eight days until the present illness which began two years ago. The only significant fact in her marital history was that she had two pregnancies twelve and fourteen years ago which terminated in full-term, normal deliveries. Her present illness started two years ago with metrorrhagia. For the past two months the bleeding had been continuous.

Physical examination was essentially negative except for the pelvic findings. Pelvic examination revealed a chronic cystic cervicitis, with an irregular and enlarged corpus the size of a fist. The adnexa were not palpated (removed at previous operation).

Findings at the Operation.—The abdomen was opened through a median subumbilical incision. Extensive adhesions were present along the old incision. Adhesions to the abdominal wall were separated only sufficiently to obtain adequate exposure of the pelvic structures. The corpus uteri was enlarged two and one-half times and densely adherent to the left side of the pelvis. The omentum, sigmoid and bladder were incorporated in the mass. It required very careful dissection to separate the sigmoid from the uterus, in fact, it was necessary to excise some of the uterine tissue in order to avoid injury to the gut. The adherent bladder was separated from the front of the uterus. By careful dissection, the bladder, then the uterus were freed from the mass. The uterus was found to be regular but enlarged. A complete hysterectomy was done. The pedicles were ligated and the vaginal vault closed about a red rubber tube drain, Dakin size. There was no evidence of pelvic endometriosis.

The appendix, left ovary, and both tubes had been removed at a previous operation. The right ovary was somewhat cystic and contained a corpus luteum. Since the patient was only 40 years of age, the operator considered it best to empty the cyst and preserve the ovary. The abdominal incision was closed without drainage. The patient was in good condition throughout the operation. Spinal anesthesia, supplemented by gas and ether toward the end, was used. An indwelling catheter was placed in the urinary bladder.

Pathologic Examination.—Gross examination revealed a complete uterus measuring in the fixed and open state 8 by 5 by 4 cm. The cervix measured 4 cm. in diameter and 4.5 cm. from external to internal os. The portio vaginalis was covered by normal epithelium and the surface was smooth and glistening. The

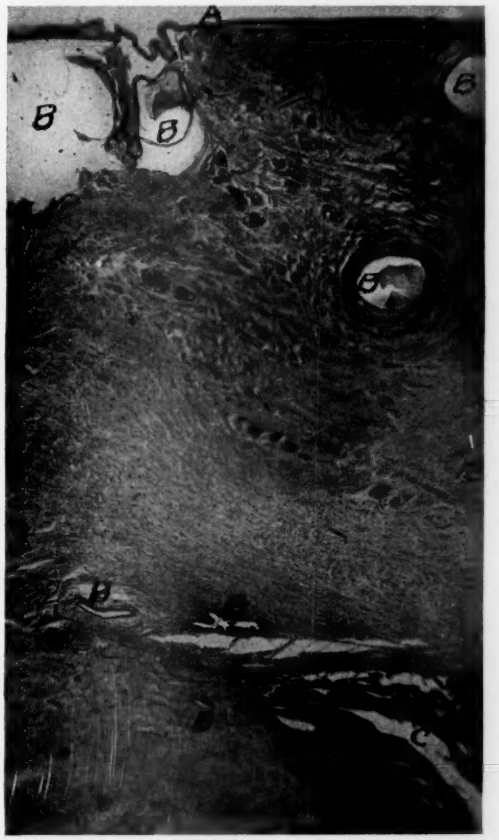

Fig. 1.—A low power photomicrograph of section taken at external os, showing squamous epithelium *A* covering the cervix; *B*, cervical glands, and *C*, an island of endometrial tissue.

cervical canal appeared normal with the exception of a small area, 0.5 cm. in diameter, located near the external os on the right side, which was brownish in color and papillary in character. There were several adhesions over the posterior surface of the corpus. The myometrium measured 2½ cm. in thickness and showed gross evidence of subinvolution. The endometrium measured 3 mm. in thickness and was rather velvety. Several blocks were taken through the cervix and the uterine wall for microscopic study.

Microscopic examination of the sections taken through the uterine wall showed normal interval type endometrium with a diffuse round cell infiltration. The

myometrium was diffusely infiltrated with round cells and the blood vessels showed changes characteristic of mild subinvolution. The sections through the portion of the cervix described as having a papillary character and brownish discoloration showed normal, stratified, squamous epithelium with many cervical glands, several of which were dilated into cystic structures (Nabothian cysts). One small area showed typical endometrial glands embedded in characteristic stroma (Figs. 1 and 2). Other sections were then taken from this area, and the same histopathologic picture was present. Many sections were taken from the posterior portion of the cervix and the uterus, and no evidence of endometrial tissue could be observed.

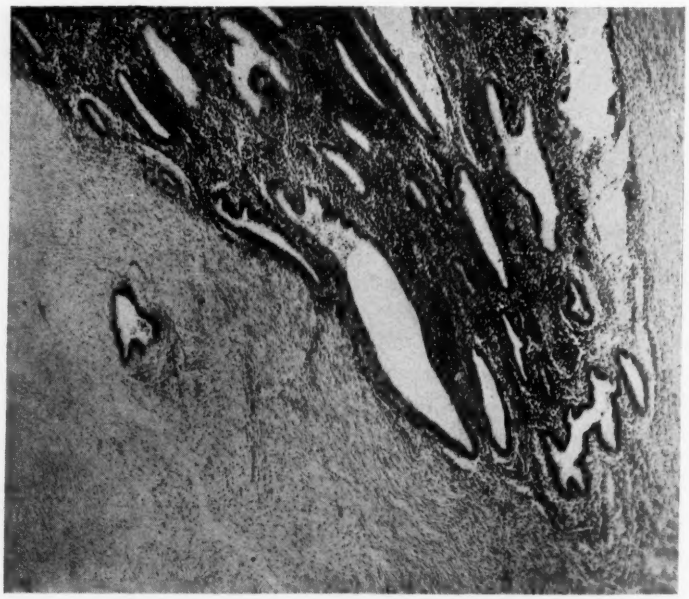

Fig. 2.—Higher power photomicrograph of area labelled *C* in Fig. 1, showing the character of the endometrium.

DISCUSSION

To us this is unequivocally a case of primary endometriosis of the cervix. We feel that the most likely explanation is that endometrial tissue became entrapped in a cervical laceration, but the possibility that it became implanted on a diseased or intact mucous membrane cannot be dismissed.

Our familiarity with the wide dissemination of endometrial tissue and the relative ease of transplantation, inadvertently at operation or experimentally, has often stimulated us to speculate on the apparent infrequent occurrence of endometriosis of the cervix, per se. The cervix is ideally situated for transplantation to occur. At each menstrual cycle, fragments of endometrium pass over the intact cervical mucosa which is apparently resistant to the growth of this tissue itself and perhaps serves as a barrier against invasion into the fibromuscular stroma. On the other hand the cervical mucosa is frequently lacerated by abortion, full-term labor, dilatation, curettage, and many other operative procedures. During a curettage, the cervical mucosa is often scraped away

to determine if a polyp or malignant growth may exist in the cervix, the fibromuscular stroma is wounded, and freshly removed, viable endometrial tissue becomes smeared over the injured surface. The fact that the lesion is so infrequent in the cervix, notwithstanding ample opportunity for implantation, justifies the obvious conclusion that the cervix is hostile to the growth of endometrial tissue. It is well known that tubal mucosa, germinal epithelium, and peritoneal mesothelium may undergo further differentiation into tissue which morphologically and functionally is identical with endometrium. These tissues have a common ancestor, the mesenchyme, and therefore, have the potentiality of developing into like tissue. The cervical mucosa is Müllerian in origin and, therefore, shares this common ancestor with the above-mentioned tissues so that the latent potentiality for differentiation into endometrial tissue exists. Three questions arise: first, does cervical mucosa ever undergo mutation into endometrial tissue? It is theoretically possible, but to our knowledge there is no evidence to support such an assumption. Second, what factor or factors inhibit this permutation in the cervix? We refrain from attempting to answer the latter question, because it would be purely speculative in nature. Third, why is the cervix so infrequently involved in primary endometriosis? We suggest a change in pH may be a factor in inhibiting the growth of endometrial tissue in the cervix. Those opposed to this theory may point out that implants occasionally occur in the vagina and perineum where there is normally a considerable change in the hydrogen ion concentration toward the acid side. Again theorizing, it may be possible that these implants occur only in the cervix, vagina, and perineum where there is an abnormally high pH due to some intravaginal disease.

SUMMARY

Endometriosis of the cervix is rare. Most of the cases that do occur are secondary to endometrial transplants in the rectovaginal septum, or are implants on the posterior surface of the supravaginal portion of the cervix. This is the second case reported of a primary endometrial transplant. Since the cervix is ideally situated for implantation to occur, the obvious conclusion is that the cervix for some unexplained reason is inimical to the growth of endometrial tissue.

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LEIOMYOSARCOMA OF THE UTERUS ASSOCIATED WITH RAMIFYING ANGIOMYOMA

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VASCULAR neoplasms of the uterus remain unusual and interesting tumors. There are at present 39 recorded cases[1] of benign hemangiomas, the majority of which have been associated with leiomyofibromata. This case is reported as an instance of a peculiar vascular process associated with a leiomyosarcoma of the uterus.

Mrs. C. R. (248,281), a 39-year-old white married housewife, was admitted to the Jersey City Medical Center on Oct. 20, 1939, complaining of profuse menstrual bleeding of nine months' duration.

Nine months before admission her menstrual flow became profuse and many clots were passed. This continued for sixteen days and was accompanied by severe cramps. Menorrhagia of a similar nature has persisted, although one or two periods were of three days' duration with but a moderate flow and less severe cramps. Four months before admission appeared a dull dragging lower abdominal pain which has been progressive. During the past three months mild headaches have accompanied her menses. Two months before admission the patient noted nocturia, two to three times, as well as infrequent dribbling with coughing or sneezing. The patient had previously been in good general health with the exception of the usual childhood diseases, and a tonsillectomy had been performed when she was 14 years of age. Five years ago she experienced an attack of epigastric pain of several days' duration, and since that time she has noted intolerance to fried or fatty foods. Her menarche occurred at 10 years of age; her periods occurred regularly each twenty-eight days, lasted three to four days, and were accompanied by moderately severe cramps. She has two healthy children and two abortions occurred at two months' and three months' gestation, respectively.

Physical examination revealed a well-developed and somewhat obese, middle-aged white female who did not appear acutely ill. The temperature was 98.6° F., the pulse 78, respiration 22, and blood pressure 112/80. The general physical examination was essentially normal. The abdomen was obese and lower abdominal striae were present. There was slight tenderness in the left lower quadrant without rebound tenderness or rigidity. A firm irregular, 5 cm. mass was felt directly above the symphysis. Pelvic examination disclosed cervical erosions and lacerations. The uterus was grapefruit in size and the ovaries were not felt.

The urinary findings were within normal limits. The hemoglobin was 70 per cent, the red blood cells numbered 3.4 million, and the white blood cells 9,200, with 63 per cent polymorphonuclear leucocytes.

Laparotomy was performed on the following day. The uterus was enlarged to three times its usual size, and irregular in contour. A 4 cm. irregular, moderately firm mass extended from the left fundal wall into the broad ligament. A total hysterectomy and bilateral salpingo-oophorectomy were performed.

The patient made an uneventful postoperative recovery and was discharged on the fifteenth hospital day. At the present time, eighteen months after her admission, large firm pelvic masses can be felt by bimanual examination.

The surgical specimen consisted of a complete uterus, two tubes, and two ovaries. The uterus measured 15 by 6 by 5 cm. Its smooth surface was interrupted by a 0.5 cm. firm pedunculated subserous mass. A somewhat softer, roughly round, lobulated, smooth, 4 cm., light pink mass was broadly attached to the left side between the peritoneal folds of the broad ligament, and smaller portions of similar tissue surrounded the lower portion of the uterus. The myometrium was 2.5 cm.

in thickness, firm and light pink. Near the periphery were several quite well-circumscribed soft, spongy, honeycombed, 0.5 to 1.5 cm., pink areas. Within the midportion was a 0.3 cm., well-circumscribed, firm, translucent, white area with a whorllike appearance. The endometrial cavity was compressed by a 3 cm. round,

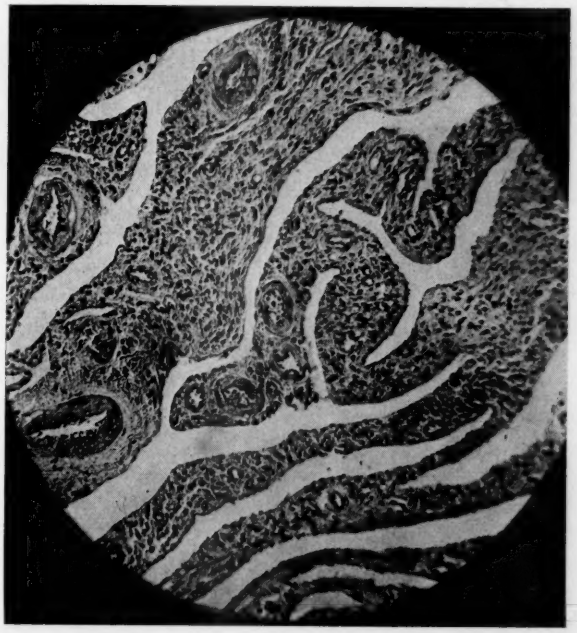

Fig. 1.—Dilated tortuous endothelial-lined tubes and a cellular stroma supporting well-developed arterioles and capillaries.

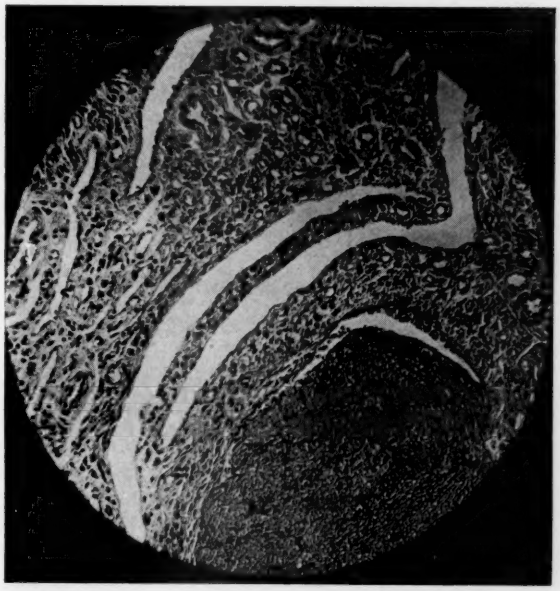

Fig. 2.—Thrombosis within one of the large vascular channels.

fairly well-circumscribed, submucous mass which was partially covered with intact endometrium and had a whorled, yellowish white cut surface with small, irregular, dark red areas of hemorrhage. The endometrium was smooth and yellowish white with a blood-tinged surface. The cut surfaces of the parauterine mass were homogeneous and light pink with small areas of hemorrhage.

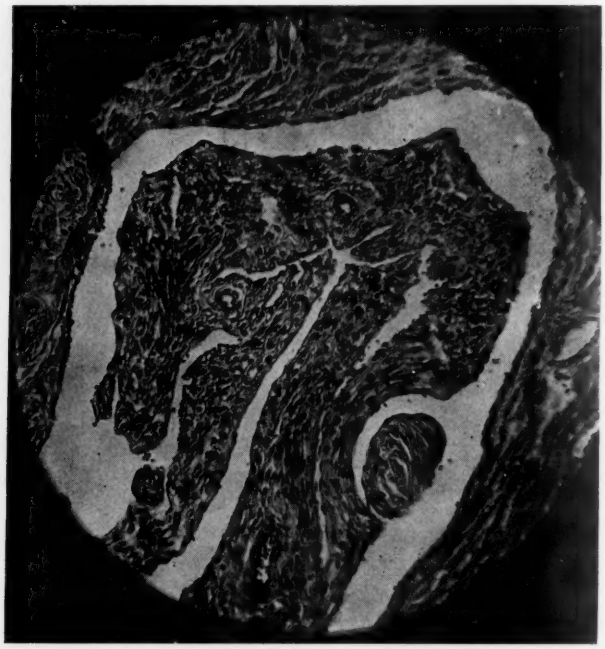

Fig. 3.—An intravascular process of elongated hyperchromatic cells supporting dilated capillaries and small arterioles.

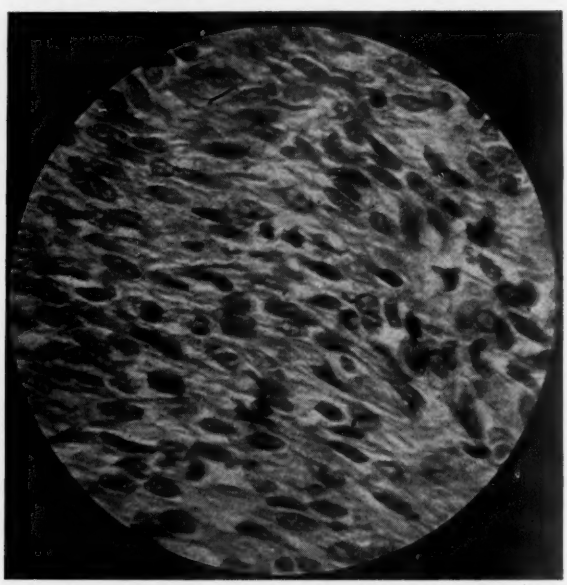

Fig. 4.—Elongated cells with hyperchromatic nuclei and mitotic figures.

Each tube measured 4.5 cm. in length and 0.8 cm. in diameter. The surfaces were smooth. On section, the musculares were well preserved, and the mucosae intact.

Fig. 5.—Bizarre multinucleated giant cells.

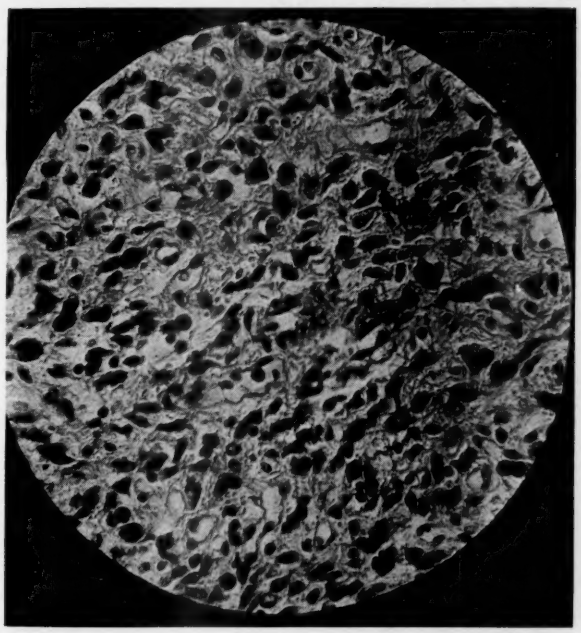

Fig. 6.—Elongated cells with scanty cytoplasm and oval nuclei rich in chromatin. Small capillary vessels are numerous.

One ovary measured 2.5 by 2 by 1 cm. On section, it presented several 0.5 cm., smooth lined cysts containing clear straw-colored fluid and a 0.5 cm. yellowish lined body filled with clotted blood supported by firm, white, ovarian stroma. The other ovary measured 3.5 by 2.5 by 2 cm. and contained similar cysts.

Microscopically, the myometrium is interrupted by several circumscribed areas composed of numerous dilated vascular channels lined by small endothelial cells (Fig. 1). Many of these spaces contain thrombi (Fig. 2). The supporting stroma contains short spindle-shaped cells, numerous small capillaries, well-developed arterioles, and areas of well-differentiated smooth muscle. Within larger channels are intravascular projections of elongated spindle-shaped cells (Fig. 3). The margin of the tumor is quite well demarcated from the myometrium. The single submucous mass is composed of closely related spindle-shaped cells with hyperchromatic nuclei which are occasionally seen in mitosis (Fig. 4) and numerous large bizarre multinucleated giant cells (Fig. 5). Sections of the parauterine mass reveal chaotically arranged, moderately acidophilic, short spindle-shaped cells with oval or elongated nuclei rich in chromatin and with a moderate number of mitotic figures. Small capillary vessels are numerous (Fig. 6). There is hyperplasia of the endometrium, the ovaries contain hemorrhagic follicular and lutein cysts, and there is moderate fibrosis of the tubes.

COMMENT

Horgan[2] distinguishes true cavernous hemangiomas from hemangiomatous fibromyomas in which circumscribed areas of greatly enlarged vessels occur only within the smooth muscle tumor. Gardner[3] uses the term "fibromyoma angiomatosum" to indicate an abundance of normally developed arteries within cellular fibromyomas.

The present case has many features similar to the ramifying angiomyoma of the uterus published by Pusch[4] in 1932. He described a 0.1 to 1.5 cm., branching, truncated mass of soft pink tissue ramifying through the myometrium from cornu to cornu and readily separated from the myometrial bed. A small, soft, red, globular structure bulged from the cut surface of the left broad ligament. Histologically the tumor was composed of conspicuous blood vessels and smooth muscle fibers arranged in cordlike structures which frequently occupied dilated venous channels. There was no fusion of the neoplasm to the adjacent myometrium.

The angiomatous tissue in our case could not be directly traced to the sarcomatous nodule. We are prejudiced to the opinion that the vascular process is independent of the leiomyosarcoma.

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Experiments on mice, infected intracerebrally with the virus of lymphogranuloma venereum and treated daily by mouth with 10 mg. per 20 Gm. mouse, showed that under the experimental conditions employed the most active compound was sulfamethylthiazole, followed by sulfapyridine, sulfathiazole, sulfanilamide, lutazeol and di-sodium 4:4′-bis-o-carboxylbenzoylamidodiphenylsulphone. Unfortunately in man sulfamethylthiazole may occasionally cause polyneuritis so that sulfapyridine remains the most effective drug clinically available. With sulfapyridine 50 of 100 inoculated animals survived in comparison to 13 survivals among 100 control inoculations.

CARL P. HUBER

THE EFFECT OF INTRAMUSCULAR INJECTIONS OF WHOLE BLOOD ON THE PROTHROMBIN INDEX OF THE NEWBORN INFANT

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THE value of intramuscular injections of whole blood in the prevention and treatment of hemorrhagic disease of the newborn infant has been questioned for many years. The history of this therapeutic procedure has been reviewed by Sanford and Leslie[1] and Quick and Grossman.[2]

Now that the majority of hemorrhagic diseases of the neonatal period have been shown to be due to deficiencies of prothrombin, it is important to measure the influence of intramuscular injections of blood upon the prothrombin indices.

Lawson[3] has recently reviewed the subject and contributed experimental evidence of the inadequacy of such intramuscular injections in raising the prothrombin levels. He reported that ten newborn infants who received intramuscular injections of their mothers' blood had levels of prothrombin during the first ten days of life which were comparable to those of ten other infants who had received no such injections.

PROCEDURE

The prothrombin clotting time was determined by the micro-technique devised by Kato as a modification of the Quick method.[4] The values were expressed in terms of prothrombin index, derived from the formula

$$\frac{\text{Normal clotting time}}{\text{Infant's clotting time}} \times 100 = \text{Prothrombin index.}$$

The blood was collected in small test tubes 7 mm. in internal diameter and 15 mm. in length instead of ground glass hollow slides. The thromboplastin* was extracted from rabbit's brain. Normal clotting time by the Kato method was 20 ± 2 seconds.

The initial prothrombin determination was made within an hour or two after the infant was born and on each of the next five days. All of the infants received the same type of feeding during the neonatal period. They were put at the breast for the first time when they were twelve hours old and at intervals of four hours thereafter.

RESULTS

The first group of 35 infants who received no injection of blood had prothrombin indices which are shown in Fig. 1.

The second group of 44 infants received 20 c.c. of their mothers' blood by intramuscular injection immediately after the first prothrombin determination was made. Their prothrombin indices are shown in Fig. 2.

To summarize these observations, averages were determined of the initial values of the prothrombin index, of the lowest values, and of the final values. In Table I,

*The thromboplastin was supplied by The Difco Co.

it will be noted that the average of the initial indices was 80.2 per cent for the untreated group and 78.2 for the group of infants who received the blood injections. The lowest average value was 37.2 per cent for the untreated group and 39.3 for the treated group. The average final value, at the end of five days, was 61.2 for the un-

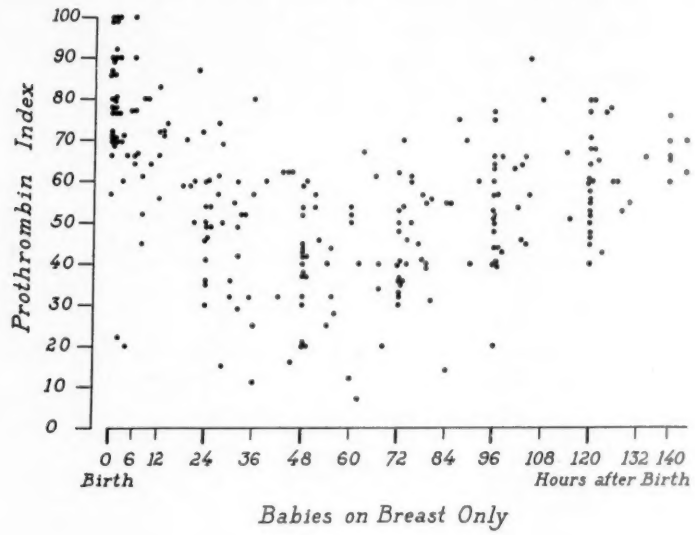

Fig. 1.

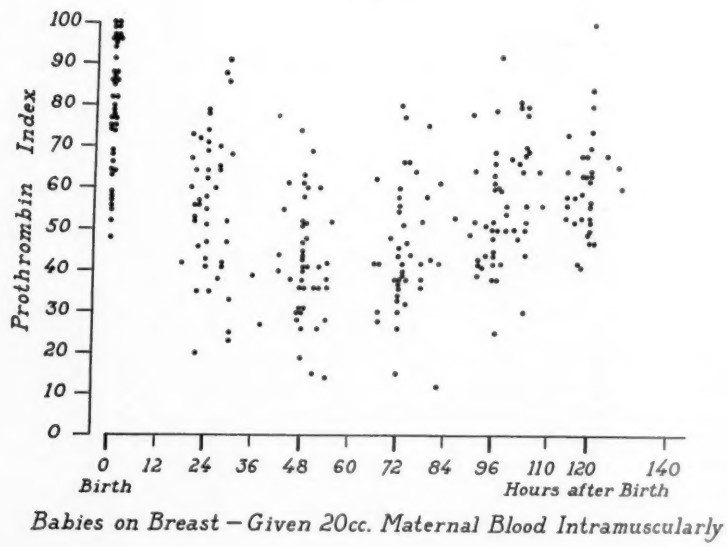

Fig. 2.

treated group and 61.6 for the treated group. These trends were generally alike with only slight advantages in favor of the group of infants who received the injections of blood. The figures of this table are shown graphically in Fig. 3.

The number of infants who regained their initial prothrombin levels and the number who reached 100 per cent by the end of five days were approximately the same in the two groups (Table II).

TABLE I. PROTHROMBIN INDICES IN 2 GROUPS OF INFANTS

	AVERAGE PROTHROMBIN INDEX		
	FIRST VALUE	LOWEST VALUE	FINAL VALUE
Group 1: 35 infants Untreated	80.2	37.2	61.2
Group 2: 44 infants Received 20 c.c. of whole blood, intramuscularly	78.2	39.3	61.6

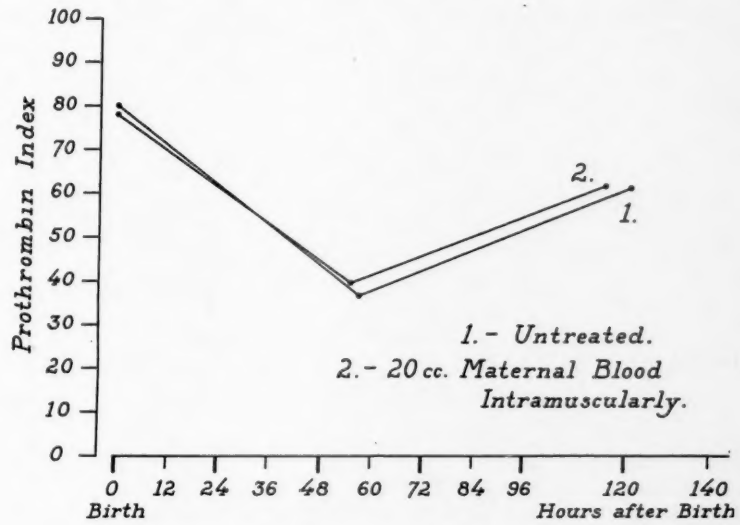

Fig. 3.

TABLE II. PATIENTS REGAINING INITIAL VALUES AND REACHING 100 PER CENT OF NORMAL WITHIN FIVE DAYS

	REGAINED INITIAL VALUE	REACHED 100%
Group 1: 35 infants Untreated	9	0
Group 2: 44 infants Received 20 c.c. of whole blood, intramuscularly	8	1

TABLE III. CHANGE IN PROTHROMBIN INDEX CALCULATED AS PERCENTAGE OF INITIAL VALUE

	MAXIMUM LOSS AS % OF INITIAL VALUE	FINAL VALUES AS % OF INITIAL VALUE
Group 1: 35 infants Untreated	52.3	78.3
Group 2: 44 infants Received 20 c.c. of whole blood, intramuscularly	49.1	81.3

When the changes in prothrombin indices were calculated in terms of the initial values, it was found that the untreated group of infants lost an average of 52.3 per cent of their initial values and returned to 78.3 per cent within the five-day period of observation. The group of infants who had received the injections of blood lost an average of 49.1 per cent of their initial values and returned to 81.3 per cent during the same period of time. The differences between the two groups was not striking (Table III).

SUMMARY

The prothrombin indices of 78 newborn breast-fed infants were determined for the first five days of life. Forty-four of these infants received intramuscular injections of whole blood and 35 did not. When the prothrombin indices of the two groups were compared, it was observed that a single intramuscular injection of 20 c.c. of maternal blood had little or no effect in checking the decline of the prothrombin index during the neonatal period, or in hastening its return to normal values.

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A PRIMARY TUBAL CARCINOMA ASSOCIATED WITH A PRIMARY OVARIAN SARCOMA

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PRIMARY carcinoma of the Fallopian tubes still stands as a gynecologic rarity. Though Renaud[1] called attention to this affection of the Fallopian tubes in 1847, it was probably Orthmann[2] who, in 1888, gave the first accurate pathologic description of this type of cancer. According to Baron[3] there were 363 cases of primary tubal carcinoma reported in the literature up to February, 1939. The incidence of primary tubal carcinoma is probably one in five to ten thousand gynecologic admissions. There has been only one other case of primary carcinoma of the Fallopian tube recorded in the files of John Sealy Hospital during the period from July, 1920, to July, 1940, from a total of 11,300 gynecologic admissions.

In making this report, we are adding another case of primary tubal carcinoma to the literature, but of greater interest is the fact that it was associated with a primary ovarian sarcoma. We are unable to discover the report of a similar case in the literature, and we offer no speculation as to why these two types of rare malignancy should occur together in the same individual.

CASE RECORD.—Patient F. C., a 39-year-old married negro woman entered John Sealy Hospital on March 22, 1940, complaining of soreness and a dull aching pain in the lower abdomen. Her symptoms had been present for only three weeks during which time she had been conscious of a mass in the lower abdomen. For twelve months the patient had experienced a watery vaginal discharge which necessitated the wearing of a pad most of the time. She claims to have lost 50 pounds during the eighteen-month period preceding her hospital admission, though she weighed 180 pounds on admission and showed no signs of recent loss. She had never experienced urinary or gastrointestinal symptoms, and she denied symptoms referable to the

abdominal or pelvic regions prior to her present illness. Of interest is the patient's menstrual history. Her last menstrual flow was ten weeks before her hospital admission. This was an interval of complete amenorrhea, not even a spotting of blood had been present. Her menses prior to this time had been regular in all particulars: onset at thirteen years, interval thirty days, duration four to five days. Her obstetric history showed one pregnancy ten years previously, terminating in a spontaneous abortion at four and one-half months.

Physical examination on admission revealed an obese colored female about the stated age, not apparently ill. Her temperature was 99.4° F., pulse 90, blood pressure 136/90. A large abdominal tumor was obvious, and some lower abdominal tenderness was present. Vaginal examination revealed a nulliparous introitus. The cervix was enlarged, soft, and boggy. It was smooth, symmetrical, and well epithelized. Lying in the cervical canal were particles of friable gray tissue. Bleeding occurred when a portion of this tissue was removed for histologic examination. The body of the uterus could not be defined as an independent mass. It seemed to be replaced by a hard fixed multinodular mass, which extended into each iliac fossa and to the level of the umbilicus. We felt that the patient had fibromyomas complicated by some type of degeneration or abortion, however pathologic examination of the tissue removed from the cervical canal revealed a glandular type of carcinoma which was interpreted as being adenocarcinoma of the body of the uterus.

Laboratory Findings.—The urine revealed rare red blood cells and frequent pus cells with clumping. Blood studies showed: hemoglobin 8.0 Gm.; red blood count 3,600,000; white blood count 7,900. The differential count was 79 per cent polymorphonuclear leucocytes, 18 per cent lymphocytes, and 3 per cent monocytes. An anteroposterior roentgenogram of the abdomen revealed a tumor mass to be somewhat eccentrically placed on the left side. In the lateral view a rounded tumor mass, having the appearance of a fibroid, was seen above the pelvic brim.

Operation and Findings.—The cervix was closed by suturing, preliminary to opening the abdomen. The peritoneal cavity was found to contain much old hemolyzed and clotted blood. A large, kidney-shaped tuboovarian mass (carcinoma) filled the lower abdomen. The mass apparently arose from the right side of the uterus but turned back and over the fundus, practically concealing the uterus. The mass was in contiguity with the entire right side of the moderately enlarged uterus, and was firmly adherent over a broad area to the floor of the right pelvis, as an intraligamentous tumor. There were several perforations in this large semisolid mass, through which much friable tissue passed when only slight pressure was made on its surface. There was another mass (sarcoma) lying posterior to the larger one, and it contained soft pultaceous areas which were easily broken into. A thin milky fluid extruded. No lymphatic metastases were demonstrable, and the firm clots filling the abdomen made it difficult to ascertain the presence or absence of established peritoneal growths. The operation consisted of a bilateral salpingo-oophorectomy, a supravaginal hysterectomy, and excision of a portion of adherent omentum. Removal of the cervix was thought inadvisable. Hemostasis was difficult because of the friability and vascularity of tissues. The abdomen was closed without drainage.

The patient was given 600 c.c. of citrated blood following the operation. Her postoperative course was essentially uneventful. On the eleventh postoperative day, intensive deep x-ray therapy was started. Six weeks following the operation viable cancer tissue was found at the external cervical os, so 3,000 mg. hours of radium was given by tandem into the cervical canal. The patient was in good health at the end of twelve months and was showing no evidence of recurrence. We consider her chances for a five-year survival practically nil.

PATHOLOGIC REPORT

Gross.—The specimen consisted of a supravaginally amputated uterus and both adnexa. The uterus measured 7 by 5½ by 4½ cm. The surface was covered with fibrous adhesions. The endometrium was thickened, measuring 6 mm. in its greatest

depth. There was a papillary mass of grayish red, somewhat necrotic tissue, extending downward from the right cornual area of the uterine cavity. This mass measured 33 by 10 by 5 mm. and was attached at various points to the endometrium. It protruded through the endocervical canal. Careful dissection of the right lateral angle of the uterus and the isthmus of the tube showed the papillary growth to be continuous with a large right intratubal mass. The right tube was markedly dilated throughout its entire length and measured 16 by 11 by 7 cm. in size. Its surface was gray and smooth except for a few fibrinous and fibrous adhesions. In places the wall of the tube was so thinned that perforations had occurred, and through these perforations gray necrotic tissue protruded. Cut section of the tube showed it to be completely filled with grayish pink necrotic tissue. Numerous small hemorrhages and areas of yellowish-orange necrotic tissue were scattered throughout the tumor. In places this mass was firmly attached to the inner wall of the Fallopian tube. In other regions it merely dilated the tube but was not definitely attached. Various transverse sections of the tube showed this tumor to pass through the lumen of the tube and into the uterine cavity, where it was implanted on the endometrium. The fimbriated end of the tube was sealed by fibrous adhesions.

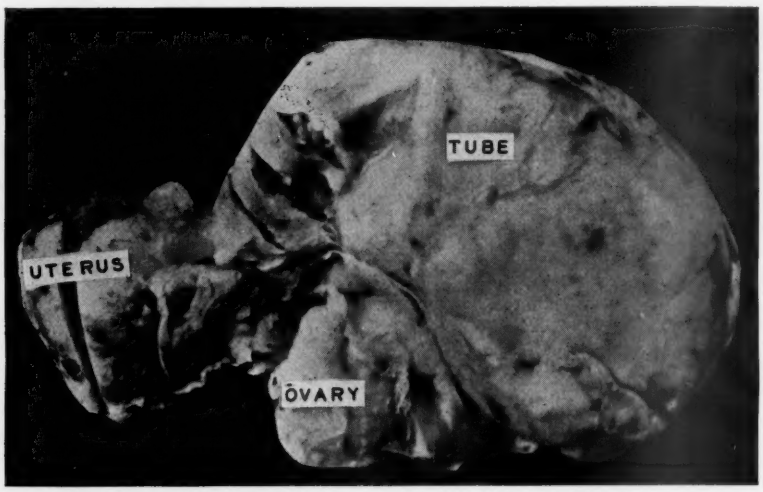

Fig. 1.—Uterus, carcinomatous right Fallopian tube, and sarcomatous right ovary viewed from the posterior side.

The right ovary was attached to the tubal mass by adhesions though separation was not difficult, the adhesions being friable and easily torn. The right ovary measured 5½ by 4 by 4 cm. and was mealy gray in color. It had an irregular consistency from firm to pultaceous. Cut section revealed several cavities that were filled with a thin milky fluid.

The left tube and ovary appeared normal, except for surrounding fibrinous and fibrous adhesions.

Microscopic Findings.—Examination of the right Fallopian tube showed it to be lined with a columnar and pseudostratified columnar epithelium. Numerous small and large papillary projections extended in all directions and completely filled the tube. In places they were compressed together and formed solid bands of epithelium with some tendency toward acini formation. Towards the central portion of the tube the tumor had apparently outgrown its blood supply, and the tissue was completely necrotic. The individual cells were generally large columnar, but varied markedly in both size and shape. Numerous mitotic figures were present, as many as four to eight being present in a single high power field. The nuclei, most of which were oval shaped, contained large amounts of diffusely scattered nuclear

material and large nucleoli. There was very little stroma present. Thin-walled blood vessels were numerous. A section of the tube through the isthmus showed a picture similar to that seen in the distal portions. The growth protruded into

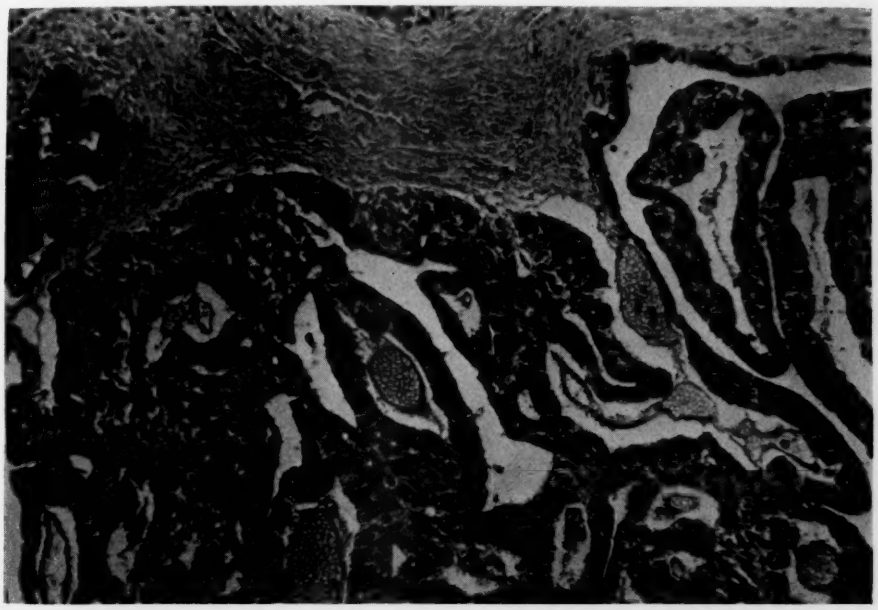

Fig. 2.—Low power of right Fallopian tube showing papillary out-growths of the carcinoma tissue.

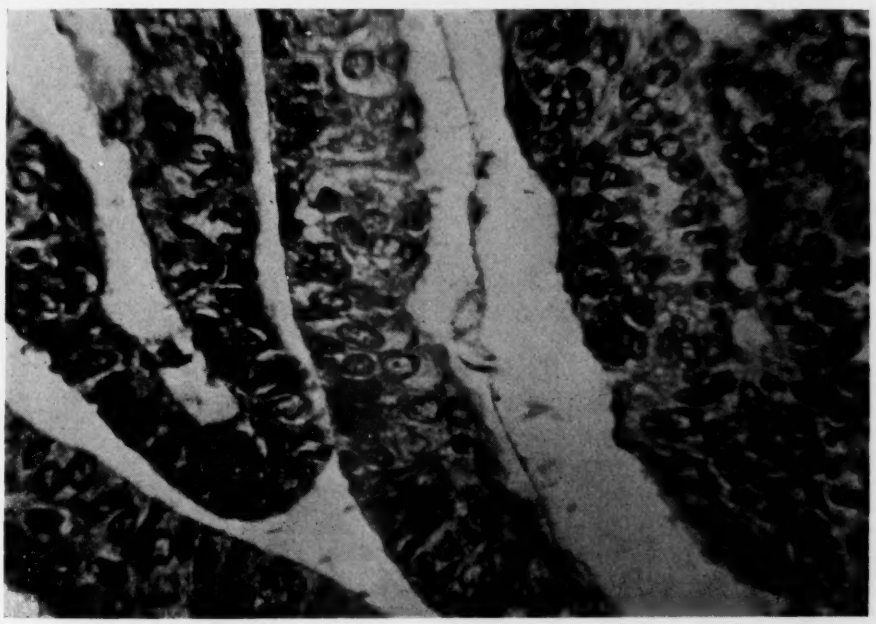

Fig. 3.—High power of the papillary carcinoma of the right Fallopian tube. Marked variation in size and shape of the cells is evident.

and occluded the lumen of the isthmus. A section through the uterus showed that the tumor had implanted on, and infiltrated into, the endometrium. The endometrial lymphatics were involved. The islands and strands of tumor cells in the uterus were similar to those seen in the Fallopian tube. The central part of the uterine papillary outgrowths was necrotic and round laminated deposits of calcium were present. A

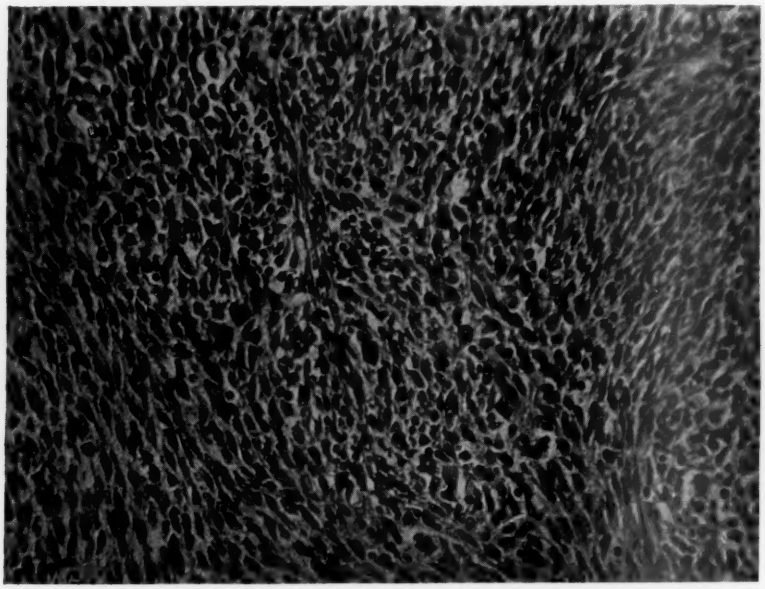

Fig. 4.—Low power of the sarcomatous right ovary. Note the tendency to form strands.

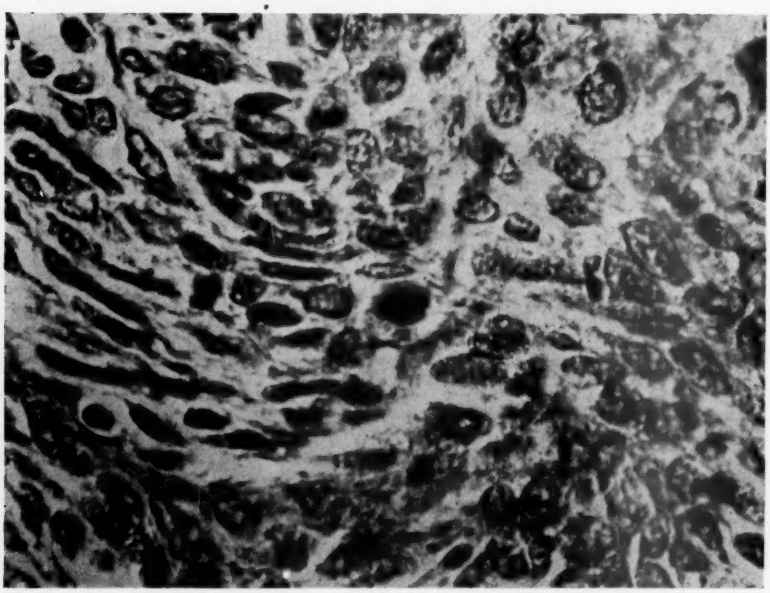

Fig. 5.—High power of the polymorphous cell sarcoma of the right ovary. The cells are large, spindle, and spheroidal shaped. Notice the numerous mitotic figures.

few fairly normal endometrial glands were present, but even these showed marked dilatation and evidence of hyperplasia.

The right ovary was composed of tissue that was entirely different from the tubal carcinoma. Running in all directions were strands of large spindle- and spheroidal-shaped cells. The nuclei contained varying amounts of nuclear material and enlarged nucleoli. Mitotic figures were numerous, there being 6 to 10 present in some high power fields. The stroma was very scarce, the entire ovary being made up of malignant cells. Numerous thin-walled blood vessels were present and in places only a single layer of edematous endothelium was present. At one point the carcinoma of the tube had invaded the sarcoma of the ovary.

The left tube and ovary were essentially normal histologically.

COMMENT

Two rare malignant tumors, a primary carcinoma of the right Fallopian tube, and a primary sarcoma of the right ovary were coexistent. To our knowledge this is the first time that this combination of malignancies has been reported.

Contrary to the usual route of spread, the carcinoma of the Fallopian tube had grown from the tube into the uterine cavity and had become implanted on the endometrium and on the mucosa of the endocervix. The carcinoma involved the lymphatics of the tube and uterus in a few isolated areas. By direct extension it had infiltrated the sarcomatous right ovary.

The microscopic picture of the carcinoma was that of a papillary type, but in the more compressed areas it had an alveolar arrangement. This agrees with Liang's[4] belief that both the papillary and the papilloalveolar type are the same morphologic tumor.

The polymorphous cell sarcoma of the right ovary was highly malignant, and the entire ovary was involved. The predominating cell was spindle-shaped, with the other cells varying markedly in both size and shape.

We wish to express our appreciation to Dr. L. L. Griffin and Dr. Gus Eckhardt for their aid with the photomicrographs.

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Rutherford, Robert N.: Pseudocyesis, New England J. Med. **224:** 639, 1941.

The author concludes a general study of the subject of spurious or imaginary pregnancy and a report of seven cases observed in Boston Lying-in Hospital during the last thirteen years with the following summary:

Pseudocyesis is a clinical entity that has existed unchanged in its symptomatology since Hippocrates first described it. Explanations of etiology mirror the medical thought of each generation, from the old physiologic explanation of "wind in the womb" to the newer concept that places the syndrome on a physiologic basis. The only additional aids to diagnosis have been the employment of roentgenography and of the biologic tests of pregnancy. Neither of these supersedes caution of the physician in diagnosing pregnancy. Today's treatment is identical with that of our medical forbears, except that it is garnished with psychotherapy.

HUGO EHRENFEST

INHIBITION OF LACTATION WITH STILBESTROL

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PRIOR to the synthesis of stilbestrol the suppression of lactation was frequently painful and difficult to accomplish. This study deals with the administration of stilbestrol orally in order to determine its efficacy in inhibiting lactation.

Fifty-five cases, 44 of which were primigravidas, requiring drying of the breasts were selected. Indications for the suppression of lactation were death of the fetus, breast abscess, sore nipples, etc.

Three nursing patients with severe painful engorgement were also given stilbestrol.

During the period of treatment, the patient's fluid intake was not restricted, tight binders were not employed and strong purgation was omitted.

METHOD OF ADMINISTRATION AND RESULTS

We administered 5 mg. of stilbestrol once a day for four days to 26 patients, beginning the first post-partum day before engorgement had taken place. In these cases this dosage seemed sufficient. No nausea, no increase of lochia, or other side effects were noted in this group of patients. After four days of drug therapy, the breasts were soft and not painful. In a few cases a thin watery secretion was noted, but the results were considered satisfactory.

One interesting case was a patient with diabetes mellitus whose daily insulin requirement was not affected by the use of stilbestrol. This patient was a 20-year-old severe juvenile type of diabetic whose daily insulin requirement was 40 units of protamine zinc insulin. She received 5 mg. of stilbestrol daily for four days.

No medication was administered until engorgement or lactation had taken place in 29 patients. In these cases, the average dose of stilbestrol was 5 mg. twice a day for two days followed by 5 mg. daily for two days.

In one case severe nausea and vomiting was noted after 20 mg. of the drug had been administered, necessitating discontinuation of the drug. This patient had developed a breast abscess three weeks post partum. It is interesting to note that she had suffered from nausea and vomiting to some degree throughout her entire pregnancy.

Five patients who had received infusions of glucose and three with unilateral abscess of the breast responded satisfactorily only after receiving subsequent doses of stilbestrol of 5 mg. once a day for four days.

One patient eight months post partum responded satisfactorily after 60 mg. of stilbestrol had been given. In this case engorgement subsided in thirty-six hours, pain disappeared in forty-eight hours, and complete suppression of lactation occurred in six days without any toxic symptoms.

In this group there were 3 patients who had shown signs of toxemia of pregnancy or pre-eclampsia before delivery. In none of these patients could we find any toxic effects from the drug. One of these patients received the average dose of stilbestrol from the third through the sixth post-partum day with good results. On the tenth

post-partum day, however, she developed an acute mastitis with a sudden rise in temperature to 104° F. Stilbestrol was given again for a total of 50 mg., during the next eight days. The mastitis subsided completely. This patient, therefore, received 80 mg. of stilbestrol without any toxic symptoms, despite the fact that she was a pre-eclamptic before delivery.

It was observed, also, that 8 other patients with breast abscesses required no larger dose of stilbestrol than the average. Therefore, in this group there were 21 cases in which complete drying of the breasts was carried out to our satisfaction on the average amount of stilbestrol.

In 3 cases of severe engorgement and painful breasts in the nursing mother, we administered 5 mg. of stilbestrol for two days. In these cases engorgement and pain rapidly subsided but lactation continued. Although this group is small, it seems to indicate that stilbestrol will not stop lactation in the nursing mother and is useful in painfully engorged breasts.

DISCUSSION

The dose of stilbestrol selected was arbitrary and was not based on any previous experience with the drug. Enseals and tablets were used at random. We noted that the 5 mg. tablets originally supplied for clinical investigation were apparently more efficacious than a total of five 1 mg. tablets.

Our cases included both white and colored patients from the obstetric ward of the hospital and the home delivery service. Several of our cases were complicated with high fevers due to pyelitis, upper respiratory infections, etc., but this did not seem to influence the effect and value of the drug. All of our patients have been followed up for a period ranging from one to five months.

SUMMARY

Fifty-five cases have been presented in which stilbestrol was used to inhibit or stop lactation both before and after lactation had occurred. In the average cases, a total of 20 mg. was used in the nonengorged and 30 mg. in the engorged or lactating breasts. The end results of both procedures were satisfactory. Abscess formation in the engorged breasts, as well as excessive amounts of fluid by the intravenous route and prolonged lactation, seemed to necessitate an additional amount of drug therapy.

Three cases of severe painful engorgement of the breasts in the nursing mother responded favorably to 10 mg. of the drug without inhibiting lactation.

In one case of a severe juvenile diabetic, the administration of stilbestrol did not affect the insulin requirement. Since the report of the use of estrin to reduce the insulin requirements of diabetics, further study of the effects of stilbestrol (synthetic estrin) on diabetic patients will be interesting to observe.

CONCLUSION

1. Stilbestrol by the oral route has been efficacious in 54 cases (98 per cent) to inhibit lactation.

2. An average dose of 20 mg. in the nonengorged breasts and 30 mg. after engorgement or lactation appeared to give satisfactory results without supportive treatment in 81 per cent of the cases.

3. Some complicated cases (17 per cent) will require additional therapy with the drug.

4. Nausea and vomiting in one case (2 per cent) was the only toxic effect of the drug noted.

5. Stilbestrol will alleviate pain and engorgement in the nursing mother without inhibiting lactation.

6. Pre-eclampsia and toxemia of pregnancy before delivery do not contraindicate the use of stilbestrol.

7. In one case, stilbestrol did not affect the daily insulin requirement of a severe diabetic patient.

Stilbestrol supplied through the courtesy of Eli Lilly Co.

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A ROENTGENOLOGIC SIGN FOR THE DETECTION OF PLACENTA PREVIA

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(From the Department of Radiology of the Presbyterian Hospital and the College of Physicians and Surgeons, Columbia University)

THE location of the placenta has been shown ante partum with the aid of roentgenography in the following manner: (1) by the injection of absorbable radiopaque media into the amniotic cavity;[1-3] (2) by the injection of colloidal thorium dioxide intravenously;[4, 5] (3) by the use of radiopaque media in the urinary bladder;[6-12] and (4) by roentgenograms of the abdomen to show the soft tissue shadows of the uterus which may be combined with the injection of air into the urinary bladder or rectum.[13-18] The first two procedures should not be used on human beings, because in (1) abortions are produced, and in (2) the radioactive substance is not eliminated from the body.

The roentgen sign herein reported is based on the fact that a fetal head will dip into the pelvic inlet and occupy the midcoronal and midmidsagittal planes of the superior strait when the mother is standing. It is applicable only in cases with a single fetus in cephalic presentation. This will include about 95 per cent of pregnancies. Any pelvic tumor mass of sufficient size can displace the fetal head from the midcoronal or midsagittal plane or prevent it from dipping below the level of the brim of the inlet. Such a mass might be a uterine fibroid, an ovarian cyst, an overdistended bladder or rectum, or the placenta implanted low in the uterus. All except the latter can be ruled out by the usual methods of examination.

TECHNIQUE OF EXAMINATION

Roentgenograms of the pelvis are taken in anteroposterior and lateral views with the patient standing. A vertical Potter-Bucky diaphragm is used. A convenient anode-film distance is 36 inches. Cassettes holding 14 by 17 inch films are used in order to include the shadow of the fetus and uterus. In the lateral view the central

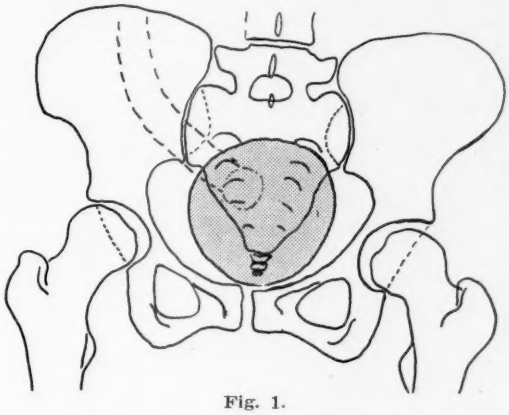

Fig. 1.

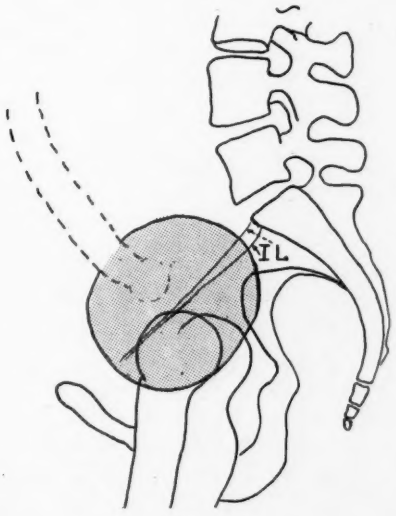

Fig. 2.

Figs. 1 and 2.—Tracings of roentgenograms taken in anteroposterior and lateral views of a woman in the thirtieth week of gestation standing erect. There was a history of recent vaginal bleeding. The position of the fetal head, dipping below the brim of the true pelvis and in the midsagittal and midcoronal planes, excluded the presence of a placenta previa. The position of the fetal head shown in 1 and 2 is the usual finding in roentgenograms taken with the patient standing. I L is the ileopectineal line, indicating the plane of the pelvic inlet.

rays are directed through the superior border of the acetabulum. The patient then turns 90 degrees to face the x-ray tube for the anteroposterior view. The Potter-Bucky diaphragm and tube, when not changed, are at the proper height for the second exposure. The central rays for the exposure should pass through the midsagittal plane of the pelvis. The technique is the same as that used in taking films for pelvimetry and fetal cephalometry.

In roentgenograms taken during the last ten to twelve weeks of gestation, by the technique described, the fetal head will be found normally in the midsagittal and midcoronal planes of the superior strait, and, even if not engaged, it will be dipping below the level of the brim of the true pelvis (Fig. 1 and 2). When the fetal head is not found in either the midsagittal or midcoronal planes and the lowest point

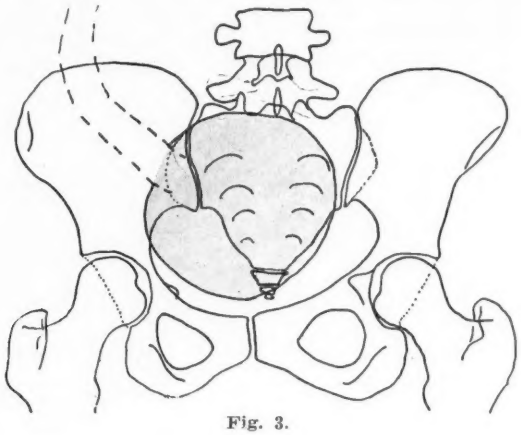

Fig. 3.

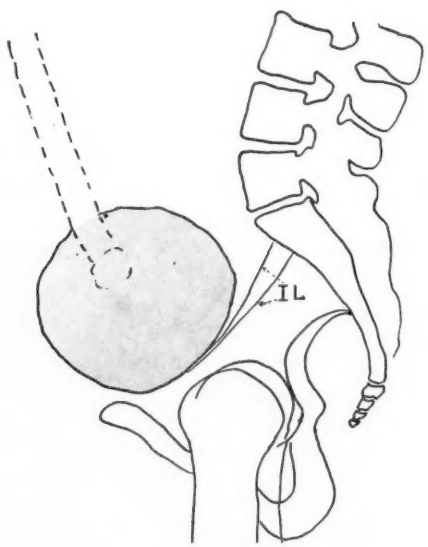

Fig. 4.

Figs. 3 and 4.—Tracings of roentgenograms taken in anteroposterior and lateral views of a woman in the fortieth week of gestation standing erect. There was no history of vaginal bleeding.

The position of the fetal head, displaced to the right of the midline and not dipping below the inlet, suggested the presence of a pelvic tumor mass.

The patient was delivered by cesarean section. The placenta was found lying over the internal os of the cervix. I L is the ileopectineal line, indicating the plane of the pelvic inlet.

of the fetal skull is at or above the level of the pelvic inlet, it indicates a displacement by a soft tissue mass in the pelvis (Figs. 3 and 4). If the pelvic mass is not due to a fibroid, ovarian cyst, or overdistended sigmoid or urinary bladder, it may be a low implantation of the placenta (placenta previa).

From our experience over a period of four years in examining roentgenograms of pregnant women, taken during the last trimester of gestation and with the patient erect, we believe any displacement of the fetal head from the midline is significant. We have accepted, for a tentative working basis, a linear displacement of one-third the diameter of the fetal head from its usual position (Fig. 1) to represent the presence of an abnormal pelvic mass. It may be that smaller degrees of displacement combined with the failure of the fetal head to dip into the superior strait will prove to be significant. One can definitely rule out the presence of a placenta previa when the fetal head is found dipping into the pelvic inlet and not displaced from the midcoronal or midsagittal planes.

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Elliott, Gillespie, and Holland, Eardley: An Outbreak of Pemphigus Neonatorum in a Maternity Home, Lancet **1:** 169, 1941.

An outbreak of skin infection resembling pemphigus neonatorum occurred in a maternity home: 22 infants, 2 mothers, and 1 nurse were affected.

Profuse, almost pure cultures of *Staph. pyogenes* were obtained from the lesions in 10 out of 11 cases examined bacteriologically and all were found to be type IIIc (Cowan).

A nurse who had two skin lesions was a nasal carrier of staphylococci of the same type. Staphylococci of this type were also recovered from plates exposed to the air during the outbreak in two wards in which were infected patients and in the nurses' dining room. These organisms were not isolated from the air of two unoccupied wards or a ward containing an uninfected patient. The evidence suggests that the nurse may have been the source and also the means of spread of the infection.

CARL P. HUBER

TWIN PREGNANCY IN THE RUDIMENTARY HORN OF A BICORNUATE UTERUS ASSOCIATED WITH RENAL AGENESIS

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THE patient, M. S. (236083), aged 26 years, had frequented the Outpatient Department since 1933, complaining of alternate periods of hypomenorrhea and amenorrhea. Several times the diagnosis of right ovarian cyst or right ectopic pregnancy had been made, but the diagnosis disqualified on further investigation. In June, 1939, a diagnosis of pregnancy was verified by the Friedman test. The date of expected labor was estimated for September 22. In September, however, the uterus was found to be only the size of an eight months' pregnancy. Her prenatal course had been uneventful until the October visit, at which time fetal heart tones were no longer heard, the patient began to lose weight and developed a two- to three-plus albuminuria, unaccompanied by hypertension. A flat plate of the abdomen revealed two fetal heads but only one fetal spine. On October 28, she began to spot vaginally, but since the spotting was not associated with pain she deferred entering the hospital until two days later. The only relevant notes in her past history were that she had had scarlet fever in her childhood and that she had received, in 1934, stimulating doses of x-ray to her ovaries and had received thyroid and ovarian substance in 1933 to 1935 for hypomenorrhea.

Examination on admission revealed a well-developed, well-nourished white female not in active labor. Temperature, pulse, and respiration were normal. Blood pressure was 128/88. Her head and neck showed no abnormalities; the lungs were clear; the heart appeared normal. In the abdomen, the uterus was the size of an eight months' pregnancy. It was quite tense but not tender. One was unable to outline definitely fetal position. No fetal heart tones were heard. Rectal examination offered no diagnostic assistance, inasmuch as both the presenting part and the cervix were out of reach. A cystogram was done and apparently was negative for placenta previa; it did, however, show two fetal heads but visualized only one fetal spine.

On October 31, the patient passed a piece of tissue grossly resembling placenta. Microscopic section revealed decidual tissue, but no chorionic villi were found. Fetal heart tones were not heard. An electrocardiogram showed no fetal heart beats. Repeated x-rays failed to reveal the second fetal spine. A sterile vaginal examination disclosed an unfavorable cervix about one inch long, which admitted only a fingertip. The presenting breech was found dipping into the inlet. No bleeding followed the vaginal examination. A medical induction, consisting of castor oil, quinine, and an enema, failed. On November 3, the Friedman test was reported as negative. When, on the next day, a repetition of the medical induction was ineffective, rupture of the bag of waters was decided upon. A sterile vaginal examination again revealed an uneffaced cervix admitting no more than the tip of one finger. The bimanual examination was confusing. A hard, fixed mass was felt on the right; a movable mass was felt on the left. An Allis forceps could not be passed beyond 1½ inches, and the examiner was unable to grasp membranes with the instrument. It was concluded that a mass was obstructing in the region of the internal os. On November 6, a flat plate of the abdomen finally revealed two heads and two fetal spines. On November 8, under gas anesthesia, the cervix was dilated with Hegar and Goodell dilators and a Voorhees' bag was inserted. The following day, the bag fell out but the

patient was not in labor. Vaginal examination at that time revealed that the dilated cervix led into a small empty uterine cavity.

On November 11, lipiodol was injected into the uterine cavity. Pictures were of no diagnostic value. Following this procedure, the patient developed a febrile reaction.

On November 20, with a preoperative diagnosis of twin pregnancy, either extrauterine or in an anomalous uterus, the patient was subjected to a laparotomy. A subtotal hysterectomy and a right salpingooophorectomy were performed.

A twin pregnancy was found in an appendage (rudimentary horn) which was attached to the right side of the main body of the uterus in the region of its internal os. The appendage measured 9 by 6¾ by 6 inches. Both fetuses were female, measured 26.5 cm. and 28.5 cm. in length, respectively, and were macerated. The umbilical cords measured 29 cm. and 25 cm. in length, respectively. The placental mass occupied most of the inner wall of the cavity. The wall of the appendage (rudimentary horn) measured 8 mm. in its thickest portion. Included in the specimen were a tube and ovary, the latter measuring 6.5 by 1.5 by 1.5 cm., which, on opening, revealed a cavity containing a small amount of red fluid blood. The uterus proper measured approximately 6.5 by 4.5 by 3.5 cm.

Fig 1.—Sketch of specimen viewed from behind, showing right tube and ovary and insertion of round ligament into rudimentary horn. The pedicle passes from the larger gravid to the nonpregnant organ.

Subserously, there were noted two hard nodular projections (fibroids), each of which measured approximately 1 cm. in diameter. The pedicle between the rudimentary horn and the uterus proper measured 3.5 cm. in length. Although no canal could be probed between the two, microscopic section revealed the presence of such communication. The round ligament on the left was attached to the uterus proper; on the right, it was attached to the anterior superior portion of the rudimentary horn. X-rays of the fetuses revealed osseous skeletal development corresponding to that of a 6½ to seven months' fetus.

The postoperative course was uneventful until the tenth day, at which time she developed an embolus with a lung infarct in the left base. One week later, having been afebrile and asymptomatic for three days, she signed her release from the hospital. Intravenous pyelograms taken shortly before her discharge showed no ureteral shadow and no dye excretion on the right. The left kidney was fairly well outlined and appeared to be normal.

The laboratory findings during her period of hospitalization were as follows:

Nonprotein nitrogen ranged from 24.0 to 33.3 mg. per cent.
Urea nitrogen ranged from 16.8 to 28.6 mg. per cent.
Creatinine ranged from 1.5 to 1.7 mg. per cent.
Total protein ranged from 7.60 to 8.36 mg. per cent.
Albumin-globulin ratio ranged from 4.51/3.09 to 5.54/3.46.
Twenty-four-hour albumin ranged from 4.28 to 12.4 Gm.
Cholesterol ranged from 125 to 187 mg. per cent.
Uric acid was 3.4 mg. per cent.
Sedimentation rate varied from 112 to 134 mm. precipitation (Westergren) in two hours.
Hemoglobin varied from 12.5 to 13.5 Gm.
White blood count varied from 18,200 to 12,200.
Urinalysis: sugar negative; albumin varied from one-plus to four-plus.

This patient was seen in December, 1940, at which time a urologic check-up was done. Cystoscopy revealed the left ureteral orifice in normal position and functioning. There was no evidence of the right orifice. A No. 6 F. ureteral catheter was passed full length on the left, releasing 3 c.c. of clear residual urine. Indigo carmine appeared from the left side in three minutes with good concentration, but there was no evidence of the right orifice in the bladder or urethra. The flat plate of the abdomen and left retrograde pyelograms showed the left kidney somewhat enlarged; the right kidney was absent.

SUMMARY

Presented herewith, because of its rarity, is a case of twin pregnancy in the rudimentary horn of a bicornuate uterus with associated renal agenesis. Gestation had progressed to approximately seven months before fetal death occurred. The uterus was unusually refractory to all attempts at the induction of labor.

In retrospect, the lipiodol injection into the uterine cavity was a procedure open to criticism.

The case illustrates typically enough the extraordinary difficulty encountered in making a diagnosis of extrauterine pregnancy.

PREGNANCY COMPLICATING HODGKIN'S DISEASE (LYMPHOGRANULOMA MALIGNUM)

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THE incidence of pregnancy complicating Hodgkin's disease is of such unusual occurrence that the following case report was deemed worthy of presentation. There are only two other cases fully reported in the literature.[1, 2]

E. S. (Bronx Hospital No. 68772), white, Jewish, aged 27 years, was referred by her family physician for obstetric care in March, 1936. She had had one previous spontaneous full-term delivery with an uneventful puerperium in 1932. Her past medical and surgical history were irrelevant. Her pelvis was of the gynecoid type; physical examination, urine, and blood pressure were normal and the Wassermann reaction was negative. After a normal prenatal course she was delivered spontaneously on Aug. 13, 1936, after a seven-hour labor of a living male child, weighing 8 pounds. Her puerperium was not remarkable and she was discharged on Aug. 22, 1936.

She was not seen again until Oct. 30, 1937, when she was readmitted to Bronx Hospital (No. 82501) because of progressive glandular enlargements of the neck

*Presented at a meeting of the Clinical Society of the Bronx Hospital, May 12, 1941.

and the left axilla during the past year, accompanied by severe itching of two weeks' duration. Positive findings on this examination were: Bilateral enlargements of the cervical and supraclavicular lymph nodes, the glands ranging in size from that of a pea to that of a small walnut. The glands were discrete and freely movable. There were also present enlarged nodes in the right axilla and left inguinal region. There was present a moderate secondary anemia with 66 per cent Hg and 4.0 million red blood cells, a mild leucocytosis of 13,000 with 80 per cent polymorphonuclears; and widening of the mediastinum by x-ray was noted.

A biopsy of one of the cervical nodes revealed Hodgkin's disease (lymphogranuloma malignum) (Path. No. 12785). Patient was discharged for radiation therapy.

During the next four weeks she received radiation consisting of 1,200 r. units in divided doses through ½ inch copper and 1 inch aluminum filter over neck and sternal regions. Her blood count remained stationary, but because of the amenorrhea and a suggestive enlargement of the uterus, a Friedman test was done, which was reported as positive. It was decided to let her continue her pregnancy because Hodgkin's disease would not preclude the development of a normal viable fetus, nor would this pregnancy endanger the life of the mother or aggravate the course of her disease.

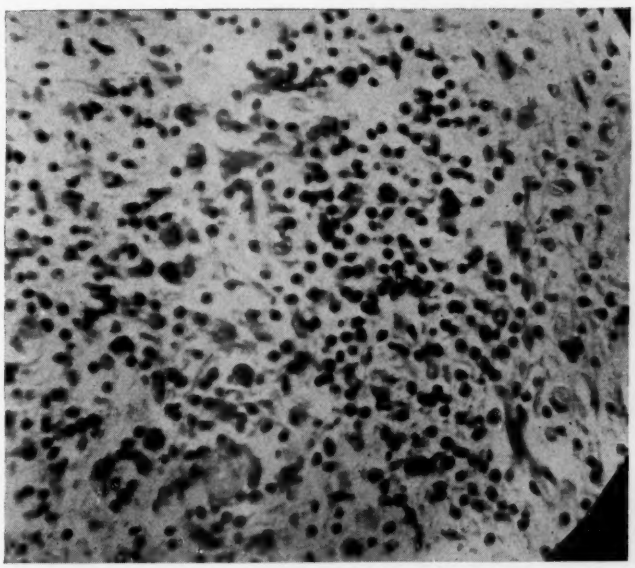

Fig. 1.—Cervical node, high power, showing the Dorothy Reed cells.

On Sept. 18, 1938, she had a spontaneous delivery of a 6 pound 2 ounce, living, normal female child. Her puerperium was uneventful and she was discharged on Sept. 27, 1938.

During the next two years, that is, until July 1, 1940, she had several divided courses of radiation (to the same areas as before), totaling 3,000 r. units. Her blood picture was maintained at a level of 70 per cent Hg with 3.8 million red blood cells by three 500 c.c. citrate transfusions during that period as well as by iron therapy orally. Suddenly, during the end of July she began to experience periods of pyrexia accompanied by a severe anemia and sudden enlargements of the cervical, inguinal, and axillary nodes. She was readmitted to the Bronx Hospital (No. 113637) on Aug. 1, 1940. Despite two 500 c.c. transfusions and 700 r. units of radiation in divided doses; her temperature ranged between 101° and 103° F., of the septic type; hemoglobin fell to 48 per cent with 2.6 million red blood cells and her condition became poor. On August 10, she was transferred to the Presby-

terian Hospital by request of the family, where she died nine days later. Necropsy confirmed generalized Hodgkin's disease (lymphogranuloma malignum).*

Follow-up studies on the baby (because of the exposure to radiation), now two and one-half years old, showed a normal development for her age.

SUMMARY

A case of Hodgkin's disease is reported, complicated by a gravidity. The patient received radiation therapy during the early months of her pregnancy. A healthy child was born, whose subsequent development was normal.

I am indebted to Dr. Meyer Rosensohn for his advice in the preparation of this report, and to Dr. Joseph Felsen for the photomicrograph.

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PLACENTA PREVIA IN THREE SUCCESSIVE PREGNANCIES

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MRS. C. G. P., aged 29 years, first consulted us on Nov. 7, 1934; her last menstruation had occurred on Sept. 14, 1934. Family history was irrelevant. She had had no previous pregnancies. Relevant in her past history was uterine bleeding which was treated unsuccessfully by two dilatations and curettages of the uterus but was successfully treated by implantation of 400 mg. hr. of radium. Her pregnancy was uncomplicated until Feb. 11, 1935, when the patient had slight, intermittent, bleeding for several months. About April 5, 1935, she developed hypertension and was kept in bed for six weeks. Spontaneous rupture of her membranes occurred on May 14, 1935, and she was hospitalized at the Norfolk General Hospital with the preoperative diagnosis of placenta previa, transverse position with ruptured membranes, and hypertension. A low cervical cesarean section was started under gas and local anesthesia. In separating the bladder from the uterus, the bladder was found to be attached intimately to the cervix and could not be separated. There were large dilated veins at this point. It was, therefore, impractical to do a typical low cervical section, so the incision was carried down to the point near the internal os from which the bladder was separable, and thence up high enough into the uterus to permit delivery of the baby. The eight months' baby was extracted by breech. He cried immediately and was placed in an incubator. The uterine wall was very thick, even down to the cervix, and gave the impression of a fibromyomatous uterus. A section of the uterus was removed for biopsy, and it showed fibrosis of the uterine muscle. After closure of the uterus, it contracted satisfactorily. The placenta had been located in the lower segment of the uterus entirely covering the cervix. Except for a few white infarcts, the placenta was grossly normal. The patient's puerperium was uncomplicated. The baby died. Autopsy showed only prematurity.

The patient continued well and became pregnant again, her last period being March 1, 1936. The pregnancy was uncomplicated until Oct. 18, 1936, when she noticed slight brownish spotting from the vagina without free bleeding. The spotting was controlled by bed rest until Oct. 23, 1936, when the patient was awakened by slight vaginal pain and found herself lying in a pool of fresh blood. She was hospitalized immediately and a modified low flap Beck cesarean section was done. The diagnosis of placenta previa with transverse lie and premature separation of the placenta was confirmed at operation. The placenta was centrally located over the internal os, and a large clot was found on its maternal surface. The 7 to 7½

*Courtesy of Dr. William C. Von Glahn, Presbyterian Hospital.

months' baby cried immediately and lived only for six hours in the Drinker respirator. Again, the puerperium was uncomplicated.

The patient continued well and returned to us on June 12, 1938, stating her last menstrual period was April 18, 1938. She was found to be pregnant. Her prenatal course was uncomplicated until Oct. 22, 1938, at which time she was given bed rest for slight elevation in blood pressure. On Oct. 29, 1938, she had a small amount of painless vaginal bleeding. The baby was lying transversely. She was hospitalized but the bleeding increased. Examination revealed a placenta previa and a transverse lie. A low modified cervical cesarean section was performed, the diagnosis was confirmed, and a dead baby of 6½ months' gestation was removed. Palpation of the uterine cavity revealed a developmental defect of the uterus. It was shaped like a bicornuate uterus with the larger horn on the right. This defect was not marked, but upon close scrutiny it made the uterus appear heart-shaped. A section of the endometrium was removed for biopsy because of its roughness. Biopsy showed masses of decidual cells with areas of necrosis. The patient's postpartum course was uneventful.

TABLE I

AUTHOR	NUMBER OF SUCCESSIVE PLACENTA PREVIA	SUSPECTED CAUSE
Binder[2]	2 placenta previa in 1 case	Not given
Mitchell[3]	2 placenta previa in 1 case	Not given (occurred in gravida vii)
Gilliat[4]	4 placenta previa in 1 case	Not given
Gilliat (Case of Fitzpatrick)	5 placenta previa in 1 case	Not given (occurred in fifth through ninth pregnancies)
Gilliat (Case of Hedback)	2 placenta previa in 1 case	Not given
Gilliat (Case of Rivett)	5 placenta previa in 1 case	Not given
MacCarthy[5]	4 placenta previa in 1 case	Not given (occurred in tenth through thirteenth pregnancies)
Deutschman[6]	2 placenta previa in 1 case	Exopthalmic goiter and uterine fibroids

A review of the literature reveals 8 cases of placenta previa occurring in successive pregnancies. To these we add our case with three successive placenta previas. In a case reported by Otero y Gama, M. (1927)[7] there were two placenta previas but not successively (in the patient's third and fifth pregnancies). Table I gives the author, the number of successive placenta previas occurring in each patient or case, and cause suspected.

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NONPUERPERAL INVERSION OF THE UTERUS

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IN THE present case there was no evidence of a recent pregnancy, the last child being delivered seven years previously. Neither were there any tumors or other masses that might have predisposed to its formation.

Mrs. F. O., aged 38 years, was received in the emergency room of the Bronx Hospital on July 18, 1940, at 5:30 P.M. She complained of vaginal bleeding in conjunction with sharp abdominal pains, intermittent in character, which had begun five hours earlier.

She had been seen at the gynecological clinic during the previous month because of vaginal bleeding. She had been told that she was three months' pregnant and was advised to have a Friedman test. She did not return to the clinic. It had been further learned though that, for a year prior to admission, she had been having metrorrhagia. During the past two weeks there was some slight abdominal enlargement and some fluid had been seeping from the vagina.

Her menstrual history was normal. She had had three children, the youngest was born seven years previously at Lincoln Hospital. There was no history of miscarriages or abortions in the interim.

Examination showed an obese adult, well developed and not in acute shock or distress. Her heart and lungs were normal. The abdomen was soft with no masses or tender areas; the liver and spleen were not palpable. Pelvic examination showed active bleeding; a corrugated mass was found to fill the upper part of the vagina. The provisional diagnosis was incomplete abortion, and the patient was taken to the operating room where she was prepared for the removal of the retained placenta.

When the vagina was exposed there was a sudden gush of a moderate amount of serosanguineous fluid and a purplish mass presented itself. This was thought to be the placenta. It was grasped with an ovum forceps and gently pulled upon, whereupon a small piece partially tore away from the mass. All manipulations were immediately discontinued and, with the patient under anesthesia a re-examination was begun. The mass was found to be purplish, edematous, and about the size of a large grapefruit. It extended upward in the form of a truncated cone, the base being wider than the apex and the cervical rim was palpated high in the vaginal vault. It was rough in contrast to the smooth feel of the vaginal mucosa. No evidence of polyps, pedunculated fibroids, or any products of conception were found. A diagnosis of inversion of the uterus then became evident and attempts were made at reposition. This proving unsuccessful, the vagina was then packed with iodoform gauze. Later attempts at reposition were again unsuccessful. The vagina was repacked and the patient was prepared for immediate laparotomy.

The abdomen was entered through a suprapubic incision. On opening the peritoneum the diagnosis was confirmed. Both ovaries and part of the tubes were in the concavity of the inversion. The iodoform vaginal packing was removed and with the assistant's hand in the vagina, efforts were made to reduce the inversion, but without success. A complete hysterectomy was then performed and iodoform gauze was placed in the vagina before its closure was completed. A cigarette drain was then placed in the cul-de-sac and the abdomen closed in the usual manner.

The patient received a citrate blood transfusion, of 500 c.c. immediately after the operation. This was followed by a continuous intravenous infusion of 2,500 c.c. of glucose (5 per cent) in saline, within the next twenty-four hours. The blood

pressure at the time of operation was 88/44. One cubic centimeter of cortate was given for shock and ¼ gr. of morphine sulphate for sedation. One hour after operation the blood pressure was 104/64, pulse 80, and temperature 100° F. On the following day, the patient was fairly comfortable, the abdomen slightly distended, and she vomited once. Prostigmin 1:2,000 had been given every four hours. She voided spontaneously after the operation. When the wound was dressed, the gauze was found to be saturated with serosanguineous fluid. On the second postoperative day the patient did not vomit, but the distention persisted, and it was necessary to institute a Wangensteen drainage. Her temperature rose steadily, reaching 103.6° F. on the third and 104.6° F. on the fourth day, although the patient stated that she was comfortable. The distention however increased. On the fifth day, at 9:50 in the morning, while the patient's bed was being changed, she complained of a sudden pain in the right side of her head. She turned over and stopped breathing. Stimulation was of no avail.

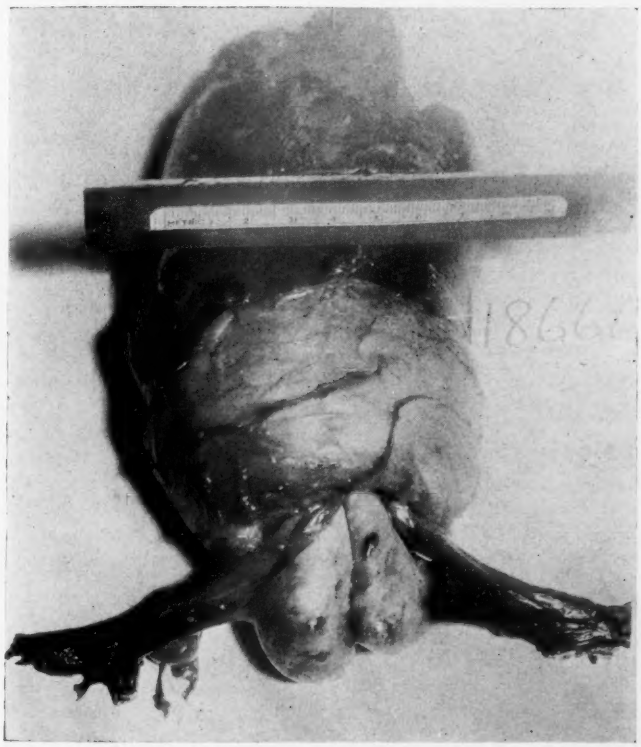

Fig. 1.—Inversion of the uterus with both ovaries and tubes (shown at bottom of photograph) being drawn into the inverted area (Accession No. 18666).

On the day of admission (July 18) her urine was negative, but on the next day showed albumin 2-plus with many red blood cells. On the twentieth the albumin was 1-plus, and there were numerous red blood cells. Her blood test on the eighteenth showed Hb, 88 per cent; white blood count, 15,500; polymorphonuclears, 79 per cent; and lymphocytes, 18 per cent. Four days later the white blood count dropped to 11,900, polymorphonuclears 86 per cent, and lymphocytes 6 per cent.

Gross Pathology (Dr. Felsen).—The specimen is an inverted uterus 17 by 9 by 7 cm. The vaginal portion consisted externally of dark hemorrhagic soft tissue, the most dependent portion of which was markedly lacerated so that portions of tissue hung from it on a pedicle. The abdominal portion consisted of a serosal area 5 cm.

in width surrounding a deep dimpling into which both tubes and ovaries had been drawn. The ovaries showed no evidence of recent corpora lutea.

Microscopically, sections showed myometrium and a small amount of endometrium characterized by diffuse edema and congestion. The outstanding feature of this tissue was the presence of widely dilated sinuses, many of which were intensely congested, some seemingly filled with blood and edematous fluid, giving the picture of an early infarction.

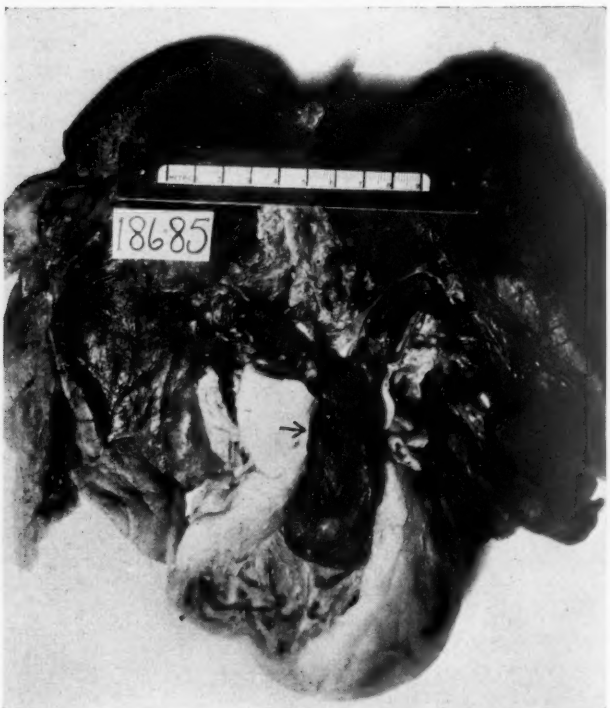

Fig. 2.—Necropsy specimen exhibiting elongated, massive, twisted thrombus, extending into both pulmonary branches from right ventricle (Accession No. 18685).

Autopsy.—Both the small and large intestines showed a generalized moderate degree of distention. There was about 1,500 c.c. of cloudy yellow fluid in the pelvis. The operative closure of the hysterectomy was complete with the sutures intact. There was no pus in the pelvis and no communication of the pelvic cavity with that of the vagina. In the great vessels of the heart, there was a massive embolus which extended from the right ventricle into the pulmonary artery, into the right and left branches, and into both lungs. The embolus was 1 by 1½ cm. wide and approximately 12 in. long, being all curled up. There was a post-mortem clot in the right ventricle separate and distinct from the embolus.

COMMENT

A case of uterine inversion is presented where the symptoms were of one year's duration and not related to pregnancy or the puerperal state. The etiologic factor was unknown. No pedunculated fibroids or other intrauterine masses were found. The sudden death was due to a large pulmonary embolus.

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MYOBLASTOMA OF LABIUM MAJUS

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MYOBLASTOMA was first described by Abrikossoff[1] in 1926. Since then about 100 cases are on record. In the series reported by Klemperer,[2] the sites of predilection are beneath the skin and mucous membranes of the tongue, maxilla, and vocal cords. Isolated instances of involvement of the breast, lip, calf of leg, and esophagus have been reported. Száthmary[4] removed one from the labium minus during a vaginal plastic operation. The authors wish to add to the growing collection of myoblastomas one that developed in the labium majus.

E. S. (Case 100-642), female, white, age 39 years, was admitted to Lebanon Hospital on the Gynecological Service of Dr. A. J. Rongy on Nov. 27, 1940, complaining of a small lump in the right labium majus. She first discovered the presence of this mass three years ago due to itching of the overlying skin. During this period the tumor has grown slightly.

The previous medical and surgical history was negative. Venereal diseases were denied. Menstruation began at 13 years, recurred regularly every twenty-eight days and lasted four days. The last menstrual period started Nov. 16, 1940. She had been delivered of two children, the first by forceps. She had one spontaneous abortion.

Physical examination revealed a well-preserved adult female not acutely ill and with no defects except in the region of the vulva. A hard, freely movable, nontender nodule about 2.5 cm. in diameter could be palpated in the anterior portion of the right labium majus immediately beneath the skin. There were no ulcerations present. No similar nodules could be found elsewhere in the body.

The blood Wassermann was negative. Hemoglobin was 74 per cent; red cells, 4,000,000; white blood cells, 7,000; polymorphonuclears, 63 per cent; lymphocytes, 33 per cent; mononuclears, 4 per cent. The urine was normal.

The clinical diagnosis was fibroma or sebaceous cyst of the labium majus.

The following day the tumor was enucleated under local anesthesia. The patient was discharged on Nov. 29, 1940. There has been no recurrence of the tumor up to the present time.

The pathologic report of Dr. Joseph C. Ehrlich follows: "Specimen 5956. Received a mass of tissue about the size of an olive. It is very firm and elastic and has the consistency of a hard rubber ball. The external surface is well delineated. It cuts with difficulty because of its marked density. On section it appears like dense connective tissue. Microscopic sections reveal this tissue to be composed of interlacing bands of broad collagen fibers between which are variously shaped groups, nests and strands of large pale cells. Some of these cells are polyhedral in form; others are band shaped. The nuclei are small and generally pale and centrally placed. The cytoplasm is very pale or invisible and contains fine granular material. There is a superficial resemblance to xanthoma cells. However, fat stains are negative. Some of the band forms contain several nuclei. The admixture of groups of pale cells and interlacing collagen fibers is uniform and extends from the connective tissue capsule to the vulvar skin surface. The histologic picture is characteristic of myoblastoma."

The appearance of a muscle tumor beneath the skin and mucous membranes, where there is normally no voluntary muscle, has given rise to much speculation as to its origin. Abrikossoff regards the tumor as the result of faulty excessive regeneration subsequent to injury. Gray and Gruenfeld[5] maintain that the cells are muscle fibers undergoing necrobiotic changes rather than a neoplastic alteration. These theories may explain the origin of the growth in sites vulnerable to injury

but cannot account for the development of the tumor in more protected regions as the esophagus, larynx, and retromammary space. Robert Meyer[3] reached the conclusion that this neoplasm results from an abnormal differentiation of the mesenchyme cells which ordinarily give rise to connective tissue. In some instances trauma may be the causative factor which starts this abnormal differentiation.

In the normal development of voluntary muscle cells, the individual cell passes from a syncytial stage to a myoblastic stage and thence to a myofibrillar stage. Godlewski, quoted by Klemperer,[2] describes the characteristic features of the myoblastic stage as consisting of large polygonal cells in ribbonlike masses with conspicuous cytoplasm free of fat. The description is essentially that represented in Figs. 1 and 2 of the mass removed from the labium majus.

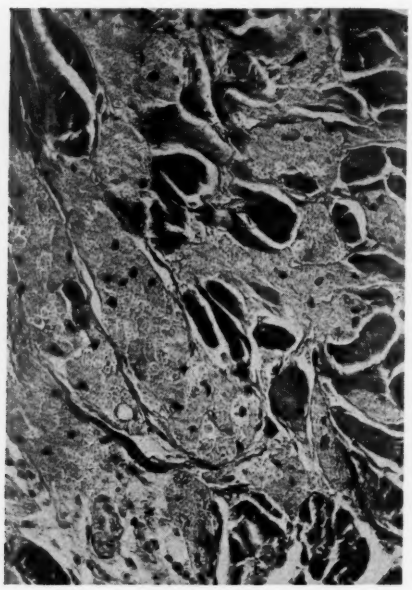

Fig. 1.

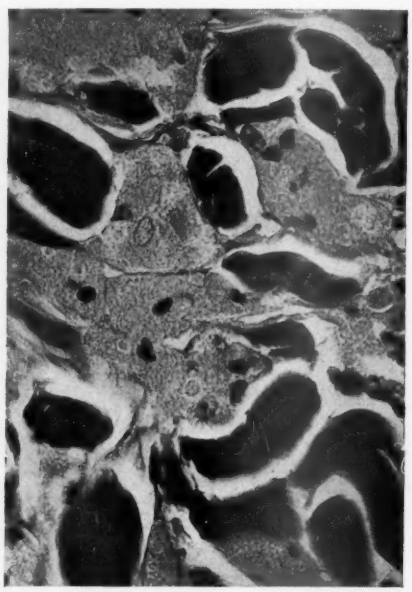

Fig. 2.

Fig. 1.—Low power. ×150. Van Gieson stain. Typical field showing interlacing collagen bundles (dark fibers) and groups of large polyhedral pale cells with granular cytoplasm.

Fig. 2.—High power. ×350. Van Gieson stain. Detail of field in Fig. 1 showing structural characteristics of nuclei and cytoplasm of the myoblasts.

Although the myoblastomas are composed of immature muscle cells, they are innocent neoplasms and should be treated with conservatism. They grow slowly, are well encapsulated, do not metastasize, and do not recur. Sarcomatous changes have been noted in rare instances.[6-8] Macroscopically the tumor resembles a fibroma or fibromyoma, but these can be differentiated readily by the histologic picture.

SUMMARY

An unusual tumor of the labium majus having the appearance of a myoblastoma is described. The mass was removed and has not recurred in six months of observation. Other cases reported since 1926 indicate the benign nature of the tumor.

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PLACENTA ACCRETA

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ONLY 118 authentic cases of placenta accreta have been reported, according to Meyer and Ashworth's[1] tabulation in 1940, after careful perusal of the literature. The incidence of this pathologic condition varies greatly: Tiemeyer[2] reports it on two occasions, a ratio of 1 in 2,156 cases; Lawson and Oginz[3] report that Polak in 34 years' experience encountered but one case in every 6,000, and that Hirst found this anomaly only once in 40,000 deliveries.

The etiology of placenta accreta is found in the partial or complete absence of the decidua basalis, allowing the villi to burrow directly into the uterine musculature, which in turn causes the placenta to be retained within the uterine cavity. Any condition producing a primary atrophy of the endometrium may be a factor in the causation of an accreta. The etiologic factors of prime importance are: previous manual removal of the placenta, too thorough curettage, endometritis, submucous myomas, previous cesarean section, and possibly dyshormonism.

The chief symptom is more or less brisk bleeding when delivery of the placenta is attempted. The diagnosis is made after an attempt at manual removal has failed to establish a cleavage plane between the placenta and the uterine musculature, thus showing retention of the placenta within the uterine cavity.

Thorough search of the literature has shown the agreement of all authorities that immediate hysterectomy is imperative as soon as a diagnosis of placenta accreta has been made. The following report is therefore presented, since treatment in this case varied so greatly from the orthodox management of this anomaly.

CASE REPORT

Mrs. R. B., aged 44 years, white, gravida xii, para xi, had no history of major illnesses. All the patient's children had been born at home and labors were easy and uncomplicated except the pregnancy just prior to the present one which had terminated at eight months in a premature stillbirth. The cause of the prematurity was unknown.

The present pregnancy was uneventful during the first two trimesters; the expected date was estimated as Sept. 22, 1932. On July 24, 1932, the amniotic sac ruptured spontaneously, and thirty-six hours later the patient was delivered normally of a live premature child at her home with the family physician in attendance.

Two hours later, after failure of the placenta to deliver and because of profuse bleeding per vaginam, the patient was sent to the University Hospital. She complained of nausea and a great deal of abdominal pain. Shock was combated by hypodermic injections of morphine and application of external heat. Later the same day, because the bleeding continued, manual removal of the placenta was at-

tempted. Only very small amounts of placental tissue could be removed and no line of cleavage could be established. At this time parenteral fluids were administered and the patient received 500 c.c. of blood by transfusion. Inasmuch as uterine bleeding continued, manual removal was unsuccessfully tried forty-eight hours after the first attempt, and the diagnosis of placenta accreta was confirmed. Because of the continuing poor condition of the patient, hysterectomy was deferred until major surgical intervention should be warranted.

A septic course ensued, with a temperature of 104° F. on the fourth post-partum day, accompanied by chills. A copious amount of foul-smelling discharge was noted throughout her hospitalization. Because of the patient's generally poor condition, accentuated by a profound anemia which did not respond to blood transfusions and liver and iron therapy, a hysterectomy was at no time thought advisable. On the tenth post-partum day her temperature and pulse began to subside and on the twenty-first post-partum day her condition warranted dismissal from the hospital. She was seen at regular intervals at the out-patient clinic where hematopoietic therapy was continued. Ten weeks later, complaining of marked backache and constant pain in the left lower abdominal quadrant, she was again admitted to the hospital. Pelvic examination showed marked relaxation of the pelvic floor and a patulous external cervical os. The uterine corpus was forward and well involuted, with some induration and tenderness in the region of the left adnexa.

A panhysterectomy, bilateral salpingectomy, and unilateral oophorectomy were performed through a midline incision by Dr. E. C. Sage. The uterus was found to be soft, of approximately normal size, and adnexal organs were normal in appearance. Upon gross examination, the cut section of the uterine corpus showed a "quite ragged endometrium but without evidence of inflammatory reaction or material which can be recognized as placental tissue."

The microscopic section, as reported by Dr. P. Tollman, showed "the endometrial surface to be covered with rather ragged masses of granulating tissue in which there are roughly circumscribed masses of very necrotic tissue which are quite uniformly pink staining. In some places this is definitely papillary in type. In a few places large and rather irregular cells remain about the border of these, which are interpreted as patchily degenerating decidual cells. This necrotic mass strikingly resembles chorionic villi undergoing degeneration. The surrounding tissue is moderately to heavily infiltrated with lymphocytes. There is an unusual amount of rather loose fibrous tissue scattered through the wall and the larger arteries show a prominent endarteritis of the type associated with atrophy of tissue." Examination of a second section was similar except for the absence of chorionic villi.

When last seen, this patient was well and had no pelvic complaints.

DISCUSSION

Careful search of the literature shows that all outstanding authorities without exception recommend immediate supravaginal hysterectomy as the treatment of choice after diagnosis of placenta accreta has been established. This procedure is augmented by transfusion both before and after surgery. Meyer and Ashworth's[1] tabulations show a mortality of 58 per cent in manual extraction or curettage; 36.4 per cent in partial manual extraction and vaginal hysterectomy; 18.9 per cent in partial manual extraction and supravaginal hysterectomy; and no mortality in supravaginal hysterectomy with no attempt at extraction.

From the mortality standpoint, this latter procedure would seem to be the method of choice. However, if no attempt at extraction is made, diagnosis is impossible because the inability to establish a line of cleavage is what differentiates placenta accreta from the simple adherent placenta. It would seem extremely radical to perform a supravaginal hysterectomy on each and every retained placenta that is not bleeding

and that has not been expelled within two hours' time, as some writers have suggested. Stander[4] warns that if a prompt hysterectomy is not done directly following the diagnosis, death from hemorrhage usually follows.

In the case presented after the diagnosis of accreta had been made, and measures to combat the acute anemia and shock resorted to, at no time during the immediate puerperium was the patient's condition sufficiently good to warrant supravaginal hysterectomy. The writer feels confident that surgical intervention would have been fatal.

At the time of the patient's readmittance to the hospital, because of her previous condition, removal of the uterus was thought advisable. But postoperative examination of the uterine corpus and the pathologic report showed that very likely no further pathologic condition of the placenta needed to be feared.

This case is reported to emphasize the successful outcome of unorthodox treatment in the immediate puerperium of placenta accreta.

REFERENCES

(1) *Meyer and Ashworth:* Virginia M. Monthly **67:** 36, 1940. (2) *Tiemeyer, A. C.:* South. M. J. **31:** 608, 1938. (3) *Lawson and Oginz:* Am. J. Surg. **41:** 70, 1938. (4) Williams Obstetrics (Stander), ed. 8, New York, D. Appleton-Century Co.

Campbell, Meredith F.: Vulvar Fusion, J. A. M. A. **115:** 513, 1940.

Fused vulva designates the condition characterized by an embryonal midline sealing together of the labia minora. As a rule an unfused area is left well forward and through this orifice the child urinates. This condition is either congenital, or acquired through inflammatory changes. The most rational explanation for the embryologic type is fusion in the midline of the labial folds, similar to that which the two scrotal folds undergo in the male, but the fusion usually lacks the density of scrotal fusion. Acquired vulvar fusion is said to follow local inflammation consequent to acute infectious diseases such as cholera, smallpox, diphtheria, scarlet fever, pneumonia, typhoid, and typhus.

The clitoris is likely to be completely covered, and the entire area appears to be all perineum. In cases of complete fusion the expulsion of urine can take place only through a congenital vaginorectal fistula or a urethrovaginorectal fistula. In other words, complete vulvar fusion in the absence of an adequate urinary exit means an unviable fetus or child. The line of fusion is well exterior to the hymenal structure. The condition is confused chiefly with hermaphroditism and pseudohermaphroditism. Hematocolpos, hematometra, and pyuria may complete the condition. Treatment consists in separation of the vulva by an incision in the cleavage line or midline of fusion.

WILLIAM BERMAN.

Society Transactions

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF MARCH 21, 1941

The following papers were presented:

The Role of Cesarean Section in the Toxemias of Pregnancy. Drs. Herman A. Strauss and Leah Fisher (by invitation). (For original article, see page 440.)

A Method for Reducing the Size of the Uterus in Vaginal Hysterectomy. Dr. A. F. Lash. (For original article, see page 452.)

The Shortening of Labor With Syntropan. Dr. John E. Stoll (by invitation). (For original article, see page 473.)

BROOKLYN GYNECOLOGICAL SOCIETY

MEETING OF MAY 2, 1941

The following papers were presented, dealing with the Causes of Puerperal Mortality in Brooklyn.

Anesthesia. Dr. Henry S. Acken, Jr.

Cardiac Disease. Dr. Thomas R. Turino.

Infection. Dr. Joseph E. Hall.

Hemorrhage. Dr. Alexander H. Rosenthal.

Cesarean Section. Dr. James L. O'Leary.

Toxemia. Dr. Frank P. Light.

Summary. Dr. Charles A. Gordon.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

The Newborn Infant

Sontag, Lester Warren: Effect of Fetal Activity on the Nutritional State of the Infant at Birth, Am. J. Dis. Child. **60:** 621, 1940.

Available evidence indicates that the system of placental transmission may limit the amount of glycogen and fatty acids available for fetal needs.

Active and frequent fetal movements require the consumption of considerable amounts of energy-producing foods which otherwise might be stored as fetal fat. Excessive fetal activity, therefore, may be responsible for considerable underweight at birth. Many factors influence fetal activity, among them sounds, maternal fatigue, or emotion.

The environment of the infant during its intrauterine life is a subject worthy of a great deal more study than is customarily bestowed.

HUGO EHRENFEST.

Gray, H., and Eder, H. L.: Big Babies and Their After-History, Am. J. Dis. Child. **61:** 717, 1941.

The frequency of births of babies weighing over 4,000 gr. has been reported as varying all the way from 1 per cent in Tokyo to 15 per cent in Esthonia. From the study of 12 such babies, the writers conclude that babies big at birth tend to continue to weigh more than average at least during the first two years of life.

HUGO EHRENFEST.

Straumfjord, Jon V.: Vernix Caseosa; a Manifestation of Vitamin A Deficiency, West. J. Surg. **48:** 341, 1940.

The author has observed patients who develop follicular keratosis during pregnancy. He notes that some mothers with this condition give birth to babies with vernix. Some doubt is raised concerning the function of the vernix. Kiupers became interested in the relationship of vitamin A to vernix. He found no noteworthy difference either in the vitamin A content of the vernices or in the incidence of the birth of babies without vernix when mothers are divided according to different economic levels.

In this report the author has attempted to influence the incidence of vernix by oral administration of vitamin A to pregnant women. Fifty thousand to 100,000 units of vitamin A were given to 25 women through six months or more of pregnancy. Twenty-one had babies with little or no vernix and 4 with moderate or much vernix. Twenty-nine women received some additional vitamin A, but much less than the women of the first group. In this group, 14 babies had little or no vernix and 15 babies had moderate or much vernix. Thirty-one women had no additional vitamin A. Eight babies in this group were born with little or no vernix and

23 with moderate or much vernix. The author feels, therefore, that vernix is abnormal and is one of the signs of vitamin A deficiency. The incidence of vernix can be influenced by the administration of vitamin A to the mother. Vitamin A is not only an antikeratinizing factor, but it is also necessary for the keratinization of the adult epidermis, and it is logical to assume that it is, therefore, necessary for fetal epidermis. Vernix caseosa is composed of the same elements as vitamin A dermatoses in the adult, and the author concludes that careful observation of a larger series of pregnant women and newborn will soon reveal that vernix is a manifestation of vitamin A deficiency.

WILLIAM BERMAN.

Ford, Norma, Ross, Mary A., and Brown, Alan: Primogeniture as an Etiologic Factor in Pyloric Stenosis, Am. J. Dis. Child. **61**: 747, 1941.

An investigation of the order of birth in 405 cases of pyloric stenosis (seen in the Hospital for Sick Children in Toronto) showed that in 50.1 per cent the patient was a first-born child. By comparison less than 41.2 per cent of the children in Toronto were first born. This difference of 10.6 per cent is shown by the writers to be statistically significant, and the importance of primogeniture as an etiologic factor in pyloric stenosis is indicated.

HUGO EHRENFEST.

Penrose, L. S.: Maternal Age, Order of Birth and Developmental Abnormalities, J. Mental Sc. **85**: 1141, 1939.

According to Penrose a positive association is demonstrable between maternal age and the incidence of mongolian imbecility, gross malformation of the nervous system, and central placenta previa. The independent effect of birth order is not easy to demonstrate conclusively. Primogeniture, however, is likely to be a significant factor in determining the incidence of gross malformation of the nervous system and of congenital pyloric stenosis. The study of maternal age and birth order usefully precedes the investigation of the genetical backgrounds of these conditions. The underlying cause of congenital pyloric stenosis seems to be a recessive diathesis. Mongolism and some other malformations may have their origin in chromosome anomalies.

J. P. GREENHILL.

Hellman, L. M., and Shettles, Landrum B.: Factors Influencing Plasma Prothrombin in the New Born Infant, Bull. Johns Hopkins Hosp. **65**: 138, 1939.

The average plasma prothrombin level in 18 mothers and 19 full-term newborn infants was 102.5 and 22.2 units, respectively.

The average plasma prothrombin level in 8 mothers and 9 premature infants was 126.9 and 8.3 units, respectively.

Preliminary studies indicate that these extremely low infant prothrombin levels can be raised by feeding vitamin K to the mother prior to delivery, or directly to the infant after birth.

C. O. MALAND.

Nygaard, K. K.: Prophylactic and Curative Effect of Vitamin K in Hemorrhagic Disease of the Newborn (Hypothrombinemia Hemorrhagica Neonatorum), Acta obst. et gynec. Scandinav. **19**: 361, 1939.

A preliminary report is presented dealing with observations on the changes in the coagulability of the blood in 54 newborn infants. The author found that the prothrombin time appears to be normal at the time of birth. From the second half of the first day to the sixth day of life, a physiologic, transitory hypothrombinemia is present. In the majority of cases of hemorrhagic disease of the newborn, the onset of hemorrhage occurs during this period. Cases in this group presenting

evidence of hemorrhage, exhibit a more marked hypothrombinemia than is normally characteristic for this stage of life. This pathologic condition has been termed hypothrombinemia hemorrhagica neonatorum.

The development of transitory hypothrombinemia appears to be successfully prevented by the administration of vitamin K right after delivery. This may eventually lead to effective prophylaxis of hypothrombinemia hemorrhagica neonatorum. Vitamin K administered to three babies with this type of hemorrhage exhibited a therapeutic effect equal to that of blood transfusion.

J. P. GREENHILL.

MacPherson, A. I. S., McCallum, E., and Haultain, W. F. T.: Effect of Intrapartum and Neonatal Administration of Synthetic Vitamin K Analogues on the Newborn, Brit. M. J. **1:** 4141, 1940.

Cord blood prothrombin index in 32 cases was found to vary widely, to be about 75 per cent of that of maternal blood, and to be unrelated to length of labor or type of delivery. Two of 5 toxemias showed marked maternal prothrombin deficiency and the cord blood showed a 15 to 20 per cent lower prothrombin index.

Prothrombin index was found to vary extremely in different individuals and in the same individuals from day to day. A decrease in prothrombin index was often demonstrated within twenty-four hours, reaching the lower level in thirty-six to eighty-four hours, then rising sharply about the fifth post-partum day to about 75 per cent. The extent of the decrease was influenced by (1) prothrombin index of the cord blood, (2) abnormal deliveries, and (3) maternal toxemia. When given a vitamin K analogue, 2 methyl—1:4 naphthoquinine in the first twenty-four hours, the prothrombin index was raised to 80 or 90 per cent and stabilized at this level for three to four days. The effect was noticeable within several hours. Administration to babies during the first twenty-four hours and to mothers during or immediately before labor, preferably twelve to four hours before delivery, gave similar results.

Association of unduly low prothrombin index, generally where there has been maternal toxemia or difficult labor, and prompt relief of cerebral symptoms on the administration of a vitamin K analogue suggests the value of further therapeutic trial.

FRED L. ADAIR AND JOHN R. KIGHT.

Fiechter, N.: Hypoprothrombinemia and Hemorrhagic Diathesis of the Newborn and Its Relation to Vitamin K, Monatschr. f. Geburtsh. u. Gynäk. **111:** 1, 1940.

By means of Quick's method, Fiechter was able to discover in the first week of life, a physiologic delay in the clotting time which was due to a deficiency of prothrombin. This normal transient disturbance in clotting time exists, to a slight degree, at the moment of birth and reaches its maximum between the third and fifth days of life. By means of vitamin K, the delay in clotting time of the newborn can be prevented. A similar effect can be produced by giving vitamin K to the mother sometime before labor. Hemorrhagic disease of the newborn also produced prolongation in the clotting time which coincides with the physiologic maximum between the third and fifth days. This prolongation in clotting time can be immediately reduced by vitamin K which at the same time stops bleeding. In the author's cases of melena neonatorum, vitamin K has replaced blood transfusion. In cases of intense jaundice, there was also a delay in clotting time. This, too, can be corrected by vitamin K.

J. P. GREENHILL.

Maumee, A. E., Hellman, L. M., and Shettles, L. B.: The Effect of Antenatal Administration of Vitamin K on the Incidence of Retinal Hemorrhage in the Newborn, Bull. Johns Hopkins Hosp. **67:** 158, 1941.

Infants with retinal hemorrhage show lower prothrombin levels than normal infants. The incidence of retinal hemorrhage in the newborn can be slightly reduced through the administration of vitamin K to mothers during labor. The prothrombin

levels are not significantly elevated in infants with retinal hemorrhage, born of mothers treated during labor. The administration of vitamin K to mothers prior to the onset of labor almost entirely eliminates retinal hemorrhage in their infants.

C. O. MALAND.

Thoms, Herbert: Observations on the Roentgenological Evidence of Fetal Death, Surg., Gynec. & Obst. **71:** 169, 1940.

At the present time there is no definite roentgenologic procedure which in all cases can be considered pathognomonic of fetal death in utero within the first week after this event has taken place. Recognizing the fact that brain collapse is an early change, our attention should be drawn to the consideration of this change in viewing roentgenograms. It may be that serial roentgenograms taken at twenty-four-hour intervals, with particular study of the fontanels and sutures, may give suggestive information concerning brain collapse, as in the case cited.

WILLIAM C. HENSKE.

Pehu and Lefebvre des Noettes: Pneumothorax in the Newborn, Rev. franç. de pédiat. **15:** 393, 1939-40.

Among the causes of neonatal pneumothorax the authors list obstetric trauma; artificial stimulation of respiration; brain lesions not due to natal traumatism, such as intracranial hemorrhages; obstructions in the trachea, such as congenital goiter and hypertrophy of the thymus; infectious disease complications, such as lobar pneumonia; accidents caused by hypodermic puncture; bronchial and cardiac malformations, and a variety of causes of undetermined origin involving fundamentally rupture of the superficial alveoli of the lungs. Pulmonary tuberculosis may be eliminated as a causative agent. Three types of neonatal pneumothorax are distinguished (partial, total, high tension) and their typical roentgenographic features are indicated. Dyspnea and cyanosis, characteristic signs of pneumothorax of the newborn, need to be diagnostically differentiated from a pathologic condition, such as normal neonatal cyanosis, those occurring in cardiovascular malformations, and from tracheal thymus pressure, bronchial or bronchopulmonary air cysts, pulmonary atelectasis and bronchopneumonia. In all of these, clinical and roentgenoscopic observations combine to disclose the real facts. Prognosis is favorable in pneumothorax of traumatic origin and in congenital bronchial malformation in which no pathologic signs manifest themselves. In high tension, pneumothorax prognosis is likewise good, provided pleural punctures succeed in preventing recurrence of air infiltration. The authors point out that the mechanism of the physiologic function of breathing when the infant first establishes independent respiration is still imperfectly understood, no elucidating roentgenograms yet existing. These mechanical factors occupy an important place in the pathogenesis of infant pneumothorax.

J. P. GREENHILL.

Paterson, J. C., and Farr, J. T.: Pulmonary Collapse as a Cause of Neonatal Death, Canad. M. A. J. **41:** 31, 1939.

From a study at necropsy of 13 stillborn infants and 12 infants who died during the neonatal period, evidence was obtained to support the belief that there is a tidal flow of amniotic fluid through the bronchial tree and pulmonary alveoli due to intrauterine respiratory movements. It is suggested that the lungs of newborn human infants contain potentially obstructing masses derived from the solid elements of amniotic fluid which may become actively obstructive if the respiratory activity is inadequate. Pulmonary collapse in the newborn appears to result from the absorption of the alveolar air entrapped distal to a point of obstruction by amniotic fluid debris.

Underlying causes of inefficient respiratory movements immediately after birth and during the neonatal period are prematurity, respiratory depression by excessive antepartum analgesia, prolonged anesthesia, and pressure from cerebral hemorrhage. Suggested treatment includes prophylaxis against these underlying causes with routine treatment directed at aiding removal of amniotic fluid debris from the lungs by postural drainage, bronchial and tracheal catheterization under laryngoscopic control, and increasing the depth of respiration by use of a respirator. Oxygen should be administered through a nasal catheter rather than by the use of the mask type of inhalations which the authors believe may result in absorption collapse of the lungs due to the absence of inert gases in pure oxygen or carbon dioxide-oxygen mixtures.

CARL P. HUBER.

Fisher, John H.: Spontaneous Pulmonic Interstitial and Mediastinal Emphysema in an Infant, Canad. M. A. J. 44: 27, 1941.

Interstitial emphysema of the lungs and mediastinum probably occurs more frequently than is at present recognized although it seldom produces a fatal outcome. In this paper the author describes an infant, born spontaneously at term, who died of increasing respiratory embarrassment within five and three-fourths hours. Respirations were normal at birth, with good color. At necropsy the left lung was largely atelectatic and small in volume. There were some interstitial emphysema and a few subpleural emphysematous blebs. These findings were more marked on the right side. Both lungs showed an accumulation of gas bubbles in the perivascular sheaths of the pulmonary vessels which was sufficient to significantly compress the vessels. It was considered that the emphysema resulted from an overinflation of the alveoli producing multiple ruptures and an escape of air into the perivascular sheaths. It is probable that this resulted in this case from a failure of normal expansion of the left lung with compensatory overinflation of the right lung. Fixation of the lungs in the distended position is important in studying the distribution of the escaped air and its relation to the lung structures.

CARL P. HUBER.

Kastendieck: Etiology of Congenital Torticollis, Zentralbl. f. Gynäk. **63**: 727, 1939.

Congenital torticollis or wryneck is an intra-uterine deformity and is not caused by the trauma of labor. It occurs chiefly in breech presentations but may be found in cases which present by the head. There is a tendency for some women to have repeated breech presentations, and because of this there is an indirect hereditary tendency to the development of torticollis.

J. P. GREENHILL.

Ottow, B.: Prolonged Opisthotonus in the Newborn Following Delivery in Face Presentation, Ztschr. f. Geburtsh. u. Gynäk. **121**: 39, 1940.

The occurrence of torticollis and opisthotonus following breech delivery is discussed. The known familial tendency in the former is questioned in the light of the somewhat similar circumstances seen in opisthotonus which seems to have no familial relation.

The cause of the opisthotonus which occurs occasionally when the breech or the face has persisted as the presenting part is unknown. The various theories are discussed. There may be mild and clinically undetectable abnormalities of the upper cervical vertebras. Dolichocephalus may play a part. It is not clear whether the extended head in the breech and when the face persists as the presenting part is caused by, or the result of, the opisthotonus seen after delivery. The author leans toward the view that there is some other cause for the extension of the head in opisthotonus and the flexion in torticollis with a resulting lack of normal muscle stretching and an interference with normal blood supply.

A case in which the face was the presenting part at the onset of labor and probably before, is described. The child was carefully studied and no lesion of the nervous system was found. By the use of simple orthopedic appliances the opisthotonus was gradually overcome, after about four months.

The author suggests the wisdom of overcoming the dearth of information in the literature dealing with this subject by carefully studying and reporting such material as it comes to hand.

J. L. McKelvey.

Chapple, Charles C., and Davidson, Douglas T.: A Study of the Relationship Between Fetal Position and Certain Congenital Deformities, J. Pediat. **18:** 483, 1941.

It is generally admitted that uterine wall pressure can affect the fetus in various ways and may play a role in the causation of certain congenital deformities. In this interesting and profusely illustrated contribution, the authors convincingly show that in some instances it is an abnormal fetal presentation which results in abnormal pressure leading to the specific skeletal anomaly evident at birth or soon afterwards. In this respect the hip is the most commonly affected joint.

It is emphasized by the writers that it is important to determine the "position of comfort" as a routine part of the examination of the newborn infant, both as a means of anticipation and prevention of bone and joint abnormalities and as an aid to the interpretation of existing deformities.

Hugo Ehrenfest.

Bruens, Egon: Thoughts About the Use of Sulfanilamide During Pregnancy, München. med. Wchnschr. **87:** 1213, 1940.

Bruens had occasion to treat newborn children for gonorrhea neonatorum with sulfanilamide (albucid) and other similar preparations, and although these products might be well tolerated by the adult this is not true for the newborn infant. The younger the infant the sooner do toxic signs and symptoms appear. In view of this observation he suggests clinical and experimental studies be made on possible toxic effects to the unborn child when sulfanilamide is administered to the expectant mother. Present conditions and circumstances make it impossible for him to study this problem.

C. E. Proshek.

Von Pallos, Karl: Two Cases of Sacral Teratoma, Ztschr. f. Geburtsh. u. Gynäk. **121:** 421, 1940.

Two characteristic cases of sacral teratoma in the newborn are described in detail. One of these tumors was made up of a mixture of tissue representing all three germ layers. The second showed fairly advanced development of organs, including a rudimentary extremity.

About two-thirds of these fetuses may be expected to deliver spontaneously and the rest will be handled by traction or destructive operations. A third of the babies will be born dead and a large number of the rest will not survive the first year. Living children should be promptly treated surgically because of the danger of necrosis and infection of the tumor mass.

J. L. McKelvey.

Brander, T.: Concerning the Os Fonticuli Frontalis and Its Clinical Significance, Acta obst. et gynec. Scandinav. **20:** 372, 1940.

The literature concerning os fonticuli frontalis (bone in the anterior fontanel) is based chiefly on studies by anatomists. Clinical observations were recorded in only 3 cases. One of these babies died during labor, the second died at twenty-five days, and the third was presumably normal at five weeks of age. In cases of

os fonticuli frontalis, palpation may lead to a wrong diagnosis. Brander reports a case which he kept under observation for eight months. His case proves that the bone in the anterior fontanel may lead to dystocia. The child developed bilateral cephalhematomas and the mother had a rupture of the vagina. The baby had a remarkable increase in the circumference of its head at one month of age and premature cranial closure at two and one-half months.

J. P. GREENHILL.

Gustafson, Gerald W., and Garceau, George J.: Cerebral Spastic Paralysis, J. A. M. A. 116: 374, 1941.

The authors report 185 instances of cerebral spastic paralysis with a detailed study of the labor in these cases. They feel that apnea resulting from anesthesia and analgesia played little, if any, part in this series. There was an increased tendency to cerebral injury in infants of mothers having less than twelve hours of labor. The greatest number of cases were found in women having normal spontaneous deliveries. Five cases followed cesarean section. Thirty per cent of the babies were premature. It is concluded that proper management of labor constitutes the best prevention of cerebral spastic paralysis, and that prevention and treatment of premature labor is the greatest single factor in the prevention of cerebral injury. Posterior pituitary extract continues to contribute to the incidence of cerebral spastic paralysis.

WILLIAM BERMAN.

Items

The Second American Congress on Obstetrics and Gynecology

The arrangements for the Second American Congress on Obstetrics and Gynecology to be held in St. Louis, Mo., from April 6 to 10, 1942, are progressing according to schedule. The various committees have been formed and are ready to function. The general program of meetings has been set up and meeting rooms in the St. Louis Auditorium have been assigned.

Efforts have been made to gauge the attitude of various commercial exhibitors toward the Congress with gratifying results. Especially encouraging is the interest shown by those who were not exhibitors at the First Congress in Cleveland in 1939. The floor plans for the exhibit space are being drawn up under the advice of representatives of the Medical Exhibitors Association, and the program is being arranged so that the members attending the Congress will have plenty of time to spend at the various booths and exhibits. Dr. Philip Williams of Philadelphia is Chairman of the Committee in charge of the Commercial Exhibits, while the details are being handled by Karl S. Richardson, Business Manager, in the office of the Congress at 650 Rush Street in Chicago.

The Program Committee, with Dr. E. D. Plass as Chairman and Dr. William F. Mengert as Secretary, is working with the various subcommittee chairmen who are: Dr. Ralph A. Reis, Medical Section; Miss Georgia Hukill, Nursing Section; Dr. R. C. Buerki, Hospital Section; Dr. Edwin C. Daily, Public Health Section; Dr. Clare Folsome, Educators Section.

The personnel of these committees will be announced in our next issue. The Central Program Committee met on Saturday, June 21, and progress was made in forming the general plan of the program which will conform to the following ideas: The program contemplates meetings of individual sections, of combined sessions, and of general sessions. Round table or panel discussions will be held by those sections which desire them. There will be evening sessions for the laity as well as for the members. Probably two evenings will be assigned to each type of meeting.

The subjects and speakers will be announced later. Dr. Robert L. DeNormandie is Chairman of the Committee on Public Meetings.

There will be moving picture exhibits, and it is planned to devote the first morning exclusively to registration and moving picture exhibitions. Dr. Robert D. Mussey is Chairman and Dr. M. E. Davis is Secretary of this committee.

The Committee on Scientific and Education Exhibits is headed by Dr. H. C. Hesseltine with Dr. Charles Galloway as Secretary. They are planning a larger and better exhibit than the excellent one of 1939.

The important Membership Committee is functioning under the leadership of Dr. Buford Hamilton, who has organized a Central Committee with representation of each of the five groups interested in the Congress. State membership committees are being formed in all the states so that all interested groups may be represented. There are also committees for special organizations. The Central Committee will map out the general plan for each state committee to follow. In the main, their function will be to inform the central office of the agencies and individuals in their states who should be interested in this Congress and to see that all these agencies and individuals have information relative to the meeting. These membership committees are the only liaison between the central office and their members and they should do all they can to act as coordinators between the central office and their groups. In the more populous states it may be wise to have county, city, or regional committees to function in a similar manner.

Dr. Joseph A. Baer is serving as Chairman of the Committee on Lay Publicity. The personnel of this group will be announced shortly. We are extremely fortunate in again securing the services of Mr. James C. Leary. He served us most enthusiastically and satisfactorily during the session of the First Congress. Dr. George W. Kosmak and his committee have charge of the professional publicity for the various sections and will welcome any assistance in the way of securing local publicity through avenues which reach the various professional groups. Dr. W. C. Danforth is Chairman of the Budget and Finance Committee and Dr. Goodrich C. Schauffler has appointed the following representatives to work with him on the Publication Committee: Dr. Ben Black, Ernestine Wiedenbach, Dr. Howard Taylor, Jr., and Dr. Reginald M. Atwater.

American Board of Obstetrics and Gynecology

The next written examination and review of case histories (Part I) for Group B candidates will be held in various cities of the United States and Canada on Saturday, January 3, 1942, at 2:00 P.M. Candidates who successfully complete the Part I examinations proceed automatically to the Part II examinations held later in the year.

Applications for admission to Group B, Part I examinations must be on file in the Secretary's Office not later than October 1, 1941. Applications for Group A must be in the Secretary's Office by March 1, 1942.

The general oral and pathological examinations (Part II) for all candidates (Groups A and B) will be conducted by the entire Board, meeting at Atlantic City, N. J., immediately prior to the 1942 meeting of the American Medical Association.

As previously announced in the Board booklet, this fiscal year (1941-1942) of the Board marks the close of the two groups of classification of applicants for examination. Thereafter, the Board will have only one classification of candidates, and all will be required to take the Part I and Part II examinations.

For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.